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PHYSIOLOGY AND PATHOLOGY OF THE DIGESTION OF FAT IN INFANCY

THEIR APPLICATION TO INFANT-FEEDING *

FRITZ B. TALBOT, M.D.
BOSTON

The food of infants comes in the main from two sources, human milk and cows' milk, the former being the natural food and the latter the best substitute we have when the former supply fails us. A brief description of these two milks is necessary for a clear conception of the subject.

The percentage of fat in cows' milk varies with the individual cow and the species. The milk of the ordinary grade cow, the Holstein or Ayrshire, contains 4 per cent. or less of fat, and that of the Jersey or Guernsey 4 per cent., or more, of fat. The fat is held in a coarser emulsion and separates more easily than that of human milk. There are other differences in the chemical and physical composition of the two milk-fats, but these will not be taken up in this paper.

Human milk normally contains, in round numbers, about 4 per cent. of fat; this percentage, however, may vary considerably in pathologic conditions, the extremes being 0.1 per cent.[1] and 13.7 per cent.[2] Every woman has a certain amount of fat to secrete in her milk, and, under like conditions, gives the same total day by day. The percentage of fat in the milk gradually increases in a certain definite curve from the beginning to the end of each nursing, the smallest percentages coming at the beginning and the highest at the end.[2] For example, the first part of the milk usually contains 2 per cent. of fat, and the last part 6 per cent. of fat; and the mixture of the whole amount of milk secreted in a single breast contains 4 per cent. of fat. The amount of milk secreted does not influence this curve otherwise than by making the ascent rapid or

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1. Moll: Ueber Fettvermehrung der Frauenmilch durch Fettzufuhr, nebst einem Beitrag für die Bedeutung der quantitativen Fettunterschiede für das Gedeihen der Brustkinder, Arch. f. Kinderh., xlviii, 161.

2. Forrest, M.: Ueber die Schwankungen im Fettgehalte der Frauenmilch und die Methodik der Milchentnahme zu Fettbestimmung, Arch. f. Kinderh., xlii, 1.

3. Engel: Ueber die quellen des Milch und Colostralfettes und über die bei der Milchsekretion wirkenden Kräfte, Arch. f. Kinderh., xliii, 194 and 204.

gradual.[4] Occasionally there is more fat in the first part of the milk than in the last part and the curve is just the reverse of the one just described.[5]

It is probable that the body-fat as well as the food-fat may be the source of milk-fat,[6] but it is not clear how the fat can be obtained from this source. Thiemich examined the literature on the influence of food on the quantity of fat secreted in the milk and came to the conclusion that a fat-free diet not only changed the quality of the fat, but also caused at the same time a diminution in the amount of fat in the milk. When a person is underfed, an increase in the fat in the food results in an increase in the fat in the milk,[7] but when large amounts of fat are added to a normal diet there is only a temporary increase in the amount of fat in the milk despite the excess of fat in the diet.[8] Ebstein[9] found in his clinic that many women with a fat-poor breast-milk would secrete more fat if they were given more fat in the food.

The amount of fat ingested by infants naturally depends on the amount in the milk, the amount of milk taken, and the part of the milk given. In asylums where one wet-nurse feeds two or more babies, the baby nursed first gets a milk relatively low in fat and the last one a milk relatively high in fat (possibly 6 per cent.). This fact is of great practical importance in feeding very delicate or sick babies, which are unable to digest large amounts of fat of any sort. Such babies may be given the first part of the milk which comes from the breast, or if desired skimmed drawn breast-milk. The wet-nurse is always instructed to nurse the sick baby first, and her own baby last; one of the reasons is that the sick baby does better on the weaker milk. In general, the amount of milk which

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4. Aurnhammer: Ueber die Beziehungen zwischen Milch production und Fettgehalt der Milch, Arch. f. Kinderh., 1909, li, 160.

5. Engel: Zur Methodik der Fettbestimmung in der Frauenmilch und die Methodik der Milchentnahme zu Fettbestimmungen, Arch. f. Kinderh., 1906, xliii, 181.

6. Bendix: Ueber den Uebergang von Nahrungsfetten in die Frauenmilch, Deutsch. med. Wchnschr., 1888, No. 14; Thiemich: Ueber den Einfluss der Ernährung und Lebensweise auf die Zusammensetzung der Frauenmilch, Monatschr. f. Geburtsch. u. Gynäk., 1899, ix, No. 4; Gogitidse: Vom Uebergang des Nahrungsfettes in die Milch, Ztschr. f. Biol., xlv, 353; ibid., xlv, 403; Caspari: Ein Beitrag zur Frage nach der quelle des Milchfettes, Arch. f. Anat. u. Physiol. (Suppl.), 1899, 267; Engel: Ueber das Milchfett Stillender Frauen bei der Ernährung mit spezifischen Fetten, Wien. klin. Wchnschr., 1906, No. 29, p. 898.

7. Johannessen: Studien zur Sekretionsphysiologie der Frauenmilch, Jahrb. f. Kinderh., xxxix, 380.

8. Albert, F.: Ueber den Einfluss von Fettfütterung auf die Milchmenge und den Fettgehalt der Milch, Ref. Malys Jahresbr. f. Tierchemie, xxix, 253; Henriques and Hansen: Untersuchungen über die Fettbildung im Tierorganismus nach intensiver Fettfütterung, Malys Jahresbr. f. Tierchemie, xxix, 68.

9. Ebstein: Die Verdauungsstörungen im Säuglingsalter, Ebstein-Schwalbes Handb. d. prakt. Med., 1900, ii, 299.

a baby will take decreases, the richer it is in fat.[10] This, however, does not usually hold true of sick babies, because the amount of milk they take in twenty-four hours does not increase with the lowered percentage of fat, but only with the return to health.[1] Therefore, when a baby has an acute infection, such as pneumonia, the milk mixture should be diluted as a whole; the fat should not be removed entirely from the mixture, because it has twice as much food value as either the sugar or protein, and because in such cases the presence or absence of fat does not influence the amount of milk taken. If, on the other hand, a healthy infant is given 5 per cent. or more of fat in its food, it will usually take less and less, and if the amount of fat is diminished it will eat more. Many babies get 6, 10 and even 12 per cent. of fat in the food because the milk mixtures are prescribed ignorantly or made improperly. This could be avoided by estimating the amount of fat in the milk by the Babcock method. When normal babies are upset by fat, it is the rule rather than the exception to find that they are receiving more than 5 per cent. in the food.

PHYSIOLOGY

The physiology of the digestion of fat is not simple, but certain facts have been established which throw some light on what is happening to the fat in the gastro-intestinal canal.

STOMACH DIGESTION

The motility of the stomach is influenced by many things, such as the concentration and the character of the food.[11] Nothing has so much influence on the time required to empty the stomach as variations in the amounts of fat, which delay or hasten the evacuation of food into the duodenum. When there is a large amount of fat in the food, the food is kept in the stomach longer, and when a small amount, a shorter time.[12] According to some writers,[13] the stagnation of fat has a connection with the pathologic condition of pyloric stenosis. It has been demonstrated in animals that fat delays the secretion of hydrochloric acid. Cannon has shown that the cardiac orifice remains open as long as the reaction of the cardia is alkaline; as soon as the reaction becomes acid, the cardiac orifice closes and remains so until the neighboring food components become alkaline. The pyloric valve acts in a manner directly

10. Gregor: Der Fettgehalt der Frauenmilch und die Bedeutung der physiologischen Schwankungen desselben in bezug auf das gedeihen der Kinder, Samml. klin. Vort. von Volkmann, 1901, No. 302.

11. Clark: Am. Jour. Med. Sc., May and June, 1909.

12. Tobler and Bogen: Ueber die Dauer der Magenverdauung der Milch und ihre Beeinflussung durch verschiedene Factoren, Monatschr. f. Kinderh., vii, 12.

13. Tobler: Beobachtungen über die Zusammensetzung des Mageninhalts bei kongenitaler Pylorusstenose, Verhandl. d. Gesellsch. f. Kinderh., 1907, p. 411.

opposed to that at the cardia. When the material in the antrum pylori is acid, the valve opens and *vice versa*.[14]

These two facts may be applied clinically in explaining regurgitation due to too much fat in the food. Fat delays or inhibits the secretion of hydrochloric acid, and the cardiac sphincter, or lid to the stomach, remains open so that milk can be pushed back into the esophagus by the peristaltic movements of the stomach. If the amount of fat in the food is diminished, regurgitation stops, presumably because the normal amount of hydrochloric acid is again secreted, causing the entrance to the stomach to close and the outlet to open at the proper time.

It has been assumed until recently that only the pancreatic juices contain fat splitting ferments. Sedgewick[15] found a ferment in the stomach contents of infants which is capable of splitting in the test-tube one-fourth of the fat, and in the body about 12 per cent. of the fat ingested. Ibrahim[16] found this same ferment in the mucous membrane of the stomach of both the fetus and the new-born baby, and proved conclusively that there is a very powerful fat-splitting ferment which in a 9-months old baby that had died from pneumonia split in twenty-four hours over 40 per cent. of the fat in the yolk of an egg.

Nature, however, provides that too much fat shall not be set free in the stomach at one time. This is brought about in the following manner: When the casein of milk is coagulated in the stomach, practically all the fat is entangled in its meshes. The casein surrounding it must be digested before any more fat can be reached by the digestive juices, and thus only as much fat is set free as the progress of digestion warrants.

INTESTINAL DIGESTION

When the stomach digestion is complete, the food is discharged into the duodenum accompanied by organic or inorganic acids which start the secretion of the pancreatic juice and bile.[17] Ibrahim[18] substantiated Zweifel's[19] findings that the pancreas of the fetus contains a fat-splitting ferment and that the action of this ferment is increased materially by the

14. Cannon: Am. Jour. Physiol., 1908, xxiii, 105.

15: Sedgewick: Die Fettspaltung im Magen des Säuglings, Jahrb. f. Kinderh., 1906, lxiv, 194.

16. Ibrahim, J., and Kopec, T.: Die Magenlipase beim menschlichen Neugeborenen und Embryo, Ztschr. f. Biol., München., 1909, liii, 201.

17. Baylies and Starling: Jour. Physiol., 1902, xxviii, 325; 1903, p. 174.
Laqueux: Sur la présence et la localisation de la sécrétine dans l'intestin du nouveau-né et du fœtus humain, Compt. rend. Soc. de biol., 1896, tai, 33.
Ibrahim and Gross: Zur Verdauungsphysiologie des Neugeborenen, Ref. in Deutsch. med. Wchnschr., 1908, No. 25, p. 1128.

18. Ibrahim: Neuere Forschungen über die Verdauungsphysiologie des Säuglingsalters. Verhandl. d. Gesellsch. f. Kinderh., 1908, p. 25.

19. Quoted by Ibrahim (see note 18).

addition of bile,[20] just as it is in the adult. Ibrahim was unable to find any fat-splitting ferment in the mucous membrane of the small intestine or large intestine.

ABSORPTION

There is considerable evidence that neutral fat (unsplit fat) is not absorbed as such into the intestinal wall: for example, hydrous wool fat and paraffin, which may be made into emulsions and cannot be split, are not absorbed.[21] It has also been shown by animal experimentation that the amount of fat in the chyme is directly proportional to the amount of fat split.[22] It is also taught by some that fat is absorbed both in the form of an emulsion and in the form of water-soluble soaps, neither view excluding the other. This latter view has been strengthened by the investigations of Kastle and Loevenhart[23] who demonstrated the almost universal presence of lipase in the tissues, and showed that this ferment could reverse its action. That is to say, it can synthesize or change soaps back into neutral fats as well as split neutral fats and form soaps. It is, therefore, possible that the soaps, which have been formed during digestion, may be changed during their passage through the intestinal epithelium by the reversible action of lipase back into neutral fat, because one finds neutral fat almost exclusively in the lymph-stream. Whitehead's[24] experiments on cats seem to strengthen this statement, because he found that butter-fat stained with Sudan III lost the stain during absorption (soaps will not stain with Sudan III); Sudan-staining fat was seen in the lumen of the intestine; none was seen in the intestinal epithelium and a Sudan-staining fat was again found in the lacteals of the villi.

A large part of the fat absorbed goes through the portal veins to the liver,[25] and the rest of it is carried by the lymphatics through the thoracic duct to the blood-stream, where it may be demonstrated by the ultra-microscope. It is called digestion lipemia and commences two to three hours after meals and disappears after seven to eight hours.[26] The

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20. Uffenheimer: Physiologie des Magendarmkanals beim Säugling, Ergebn. d. inn. Med. u. Kinderh. 1908, No. 2, 321.

21. Connstein, W.: Arch. f. Anat. u. Physiol., 1899, p. 30; Henriques and Hansen: Zentralbl. f. Physiol., 1900, xiv, 313.

22. Levites: Ueber die Verdauung der Fette im tierischen Organismus, Ztschr. f. physiol. Chem., xlix, 273; liii, 349.

23. Kastle and Loevenhart: Am. Chem. Jour., 1900, xxiv, 491.

24. Whitehead, R. H.: A Note on the Absorption of Fat, Am. Jour. Physiol., 1909, xxiv, 294.

25. Weinland: Physiologie der Leber, Nagel's Handb. d. Physiol., ii, Part 2, 456.

26. Ueber ultramikroskopische Blutuntersuchungen zur Zeit der Fettresorption bei Gesunden und Kranken, Wien. klin. Wchnschr., 1907, p. 851; Schelble: Untersuchungen über die Fettresorption des Säuglings, München. med. Wchnschr., 1908, No. 10; Bahrdt: Demonstration zur Untersuchung der Lipämie beim Säugling, Breslauer Tagung der Freien Vereinigung für wissenschaftliche Pädiatrie, 1908, Monatschr. f. Kinderh., vii, 107.

height of the curve is dependent on the amount of fat in the food, and the age and condition of the infant.

The absorption of fat is extraordinarily good in health in babies fed on cow's milk as well as in those fed on human milk; it is usually over 90 per cent. and may be as high as 98 per cent. of the fat ingested.[27] Eight per cent. to 11 per cent. of the ingested fat is absorbed in the upper part of the small intestine[22] and the absorption of fat is nearly complete at the ileocecal valve.[22] The large intestine is capable of absorbing fat in large amounts under special favorable conditions[28] but under ordinary circumstances absorption here is probably very little.

Estimation of the amount of fat in the stools of babies in starvation and in health makes it probable that the greater part of the fecal fat comes from the food and not from the intestinal secretions.[27] It is evident, therefore, that microscopic fat that is found in the stools gives us valuable information about the digestion. It is necessary first to know how much fat may normally be found in a stool. There is a comparatively large amount of fat present in the first days of life, and this amount gradually becomes less[29] as the babies grow older, decreasing from 50 per cent. of the dried stools to between 14 and 25 per cent. There is so much fat passed in the stools during the early weeks that it is practically impossible to ascertain by simple microscopic examination whether there is an excess or not. In later infancy less fat is present and therefore, microscopic examinations are of more value. In normal and in many pathologic conditions the greater part of the fat, 75 per cent. or more, is split by the digestive juices and bacteria into fatty acids and soaps.

A recapitulation of the facts given above is in brief as follows: most of the fat in cows' milk or human milk is in the form of neutral fat; in normal digestion this is partially split in the stomach by the gastric lipase. When the food is emptied into the duodenum, the remainder of the fat is presumably split by the pancreatic juice and saponified by the alkalies surrounding it. This digested fat is absorbed in the small intestine between the duodenum and the ileocecal valve and only the overflow fat goes into the large intestine with the intestinal secretions and bacteria. There the fecal remains are desiccated and eventually evacuated. The normal appearance of stools varies according to the food which the infant

27. Czerny-Keller: Der Kinder Ernährung, Ernährungsstörungen und Ernährungstherapie, Leipzig u. Wien, 1906, p. 263; Freund: Physiologie und Pathologie des Fettstoffwechsels im Kindesalter, Ergebn. d. inn. Med. u. Kinderh., 1909, ii, 139.

28. Hamburger, H. J.: Ueber die Resorption von Fette und Seife im Dickdarm, Engelmann's Arch., 1900, 433.

29. Talbot, F. B.: The Composition of Small Curds in Infants' Stools, Boston Med. and Surg. Jour., Jan. 7, 1909.

is taking. An excellent description of these stools may be found in a paper by Morse.[30]

STOOLS: MICROSCOPIC EXAMINATION

Much valuable information concerning the digestion of the various food components may be obtained from careful gross and microscopic examinations of the stools. This evidence is definite and accurate and is not misleading like the symptoms obtained from mothers and nurses. There are several quick methods of estimating the fat in the stool under the microscope.

1. The first consists in staining a bit of stool with saturated alcoholic solution of Sudan III. Neutral fat drops stain red. Fatty acids may be in the form of drops or crystals; the former always stain and the latter sometimes stain. Soap splinters and crystals never stain. The total fat in the slide may be estimated by adding a drop of glacial acetic acid to the already stained preparation, and warming it gently until it begins to bubble. This changes soaps into fatty acids which are red drops as long as they remain hot and often when they become cold. The error in this method comes from the fact that it is impossible to differentiate neutral fat and fatty acid drops. I have used this stain nearly three years.

2. The second method consists[31] in staining a scrap of stool with carbol-fuchsin and examining under the microscope. With this, neutral fat remains unstained, fatty acids stain a brilliant red and soaps a dull rose-red. Recently, I have used both stains, one on each of two cover-glass preparations, and thus obtained an estimate of the total amount of fat present, and the relative amounts of neutral fat, fatty acids, and soaps. Preparations from several parts of each stool should be examined in this way because the picture is apt to vary in stools which are not uniform.

The following terms are based on innumerable microscopic examinations of stools many of which were controlled by quantitative chemical analyses:

1. *Entire Digestion of Fat.*—Microscope, No. 7 objective, No. 3 eyepiece. Stain. alcoholic Sudan III. No fat in freshly stained specimen. One to three drops in field after acetic acid and heat.

2. *Normal Digestion.*—No fat or five to eight neutral fat-drops in the entire cover-glass in freshly stained specimen. Five to eight drops in a field after addition of acetic acid and heat. No change in amount of fecal residue.

3. *Slight Excess of Fat.*—No fat or two to four neutral fat-drops in a field. Eight to a dozen drops in a field after acetic acid and heat. No change in amount of fecal matter.

4. *Moderate Excess of Fat.*—No fat or six to eight neutral fat-drops in a field. More than twelve large drops after addition of acetic acid and heat. Considerable fecal material remains unchanged.

30. Morse, J. L.: The Stools in Infancy, New Orleans Med. and Surg. Jour., August, 1910.

31. Jacobson: Sur une réaction colorante des acides gras, Presse méd., 1906, No. 19, p. 147.

5. *Large Excess of Fat.*—No fat, or many fat-drops in a field. Practically the whole slide turns into fat-drops after acetic acid and heat, leaving very little fecal matter unchanged.

If there are any fat-drops in the original preparation it should always be stained with carbol-fuchsin to differentiate neutral fat from fatty acids. The entire cover-glass should be examined and it is usually better to examine preparations from several parts of the stool.

The following deductions can be drawn from these findings:

1. *Entire Digestion of Fat.*—It is always safe to increase the amount of fat in the food if so desired.

2. *Normal Digestion.*—It is usually safe to give more fat if necessary.

3. *Slight Excess of Fat.*—It is difficult to say how much significance should be attached to this. Probably very little.

4. *Moderate Excess of Fat.*—Without symptoms of indigestion it warns the observer to watch the fat more carefully. Yet, curiously enough, the percentage of fat may be increased without causing symptoms of indigestion and subsequently the stool may show "normal digestion." In case there are symptoms of indigestion, however, the microscope confirms our suspicions, and indicates the cause of the symptoms.

5. *Large Excess of Fat.*—This always means too much fat in the food and even if there are no symptoms, it is safer to decrease the amount of fat and examine the stool again. Usually there are symptoms of indigestion with this microscopic picture.

Fat is usually found in a normal stool in some form or other. Neutral fat appears as drops of different size and shape and sometimes as irregular flakes. When there is a very large amount it may be seen with the naked eye; it may be colorless, yellowish or slightly bile stained.

Free fatty acids may be indistinguishable from neutral fat drops except by staining with carbol-fuchsin. Neutral fat drops do not stain, while fatty acids stain; the more intense red the more acid they contain. When they are in the form of crystals, gentle warming will cause them to become drops, which recrystallize on cooling. Soaps may be amorphous or in the form of crystals. They are less shiny than fatty acids and may be stained yellow with bile coloring matter. The bushel-stained soap crystals may be in clumps and are shorter and thicker than fatty acids.

The microscopic examination of the stools of babies only occasionally gives information that the gross examination does not give, but it is a valuable control to inspection. In a few instances, the information is very surprising. It is important to bear in mind that even with considerable microscopic fat, a baby can remain perfectly happy, continue to gain and have no symptoms. This information, therefore, should be taken with reserve. In childhood, when foods other than milk are taken, small amounts of microscopic fat are of more significance. During the third year there should be only a few fat-drops on the whole slide in a normal digestion. More means a disturbance in the digestion of fat.

The closer a child comes to the adult type of diet, the more significance can be attached to information given by the microscope.

MACROSCOPIC EXAMINATION

The gross examination of the stool is the more important because it gives the most valuable information. The commonest abnormal constituents in a stool are soft, fatty curds. Soft curds are either flat white flakes (which look like undigested milk particles) or pin-head elevations; both may be present in the same stool and they are always associated with more or less mucus, which is stained green or yellow. About 60 per cent. of their dried substance is fat. These curds are usually present at one time or other in the stools of all nursing babies and are of no significance even with slight symptoms of indigestion. They are more important in the stools of bottle-fed babies. If there are no symptoms of indigestion and the baby is gaining and happy, the percentage of fat should not be changed, but the significance of these curds should be remembered. If there are symptoms of indigestion, loss of weight, and soft, fatty curds in the stools, there is too much fat in the food. When it is diminished, the curds disappear, the baby becomes happy and gains weight.[32]

These curds should not be confused with tough casein curds, which are white or bile-stained, bean-like masses of varying size and shape. They may be easily differentiated from the fat curd by their physical characteristics. The latter will smooth out on a napkin while the former will not; casein hardens in liquor formaldehydi (formalin) while fat does not. I recently proved [32] by the precipitin reaction that the protein in these curds is cow-casein. They contain varying amounts of neutral fat which is entangled in the meshes of the casein when it coagulates in the stomach. This fat has not been acted on by the digestive juices because it is protected by a coating of casein. It is present in larger or smaller amounts, according to the percentage of fat in the milk and may, therefore, be considered accidental.[33]

Soap stools are very light yellow or white, usually smooth, sometimes salve-like, at other times dry and brittle. The shiny appearance of the fresh surface suggests fat. They are composed almost entirely of soap. Fifty per cent. to 70 per cent. of their dried substance may be fat. They often occur in constipation due to too much fat in the food and disappear when the fat is replaced by other food components. They may be the precursors of a fat diarrhea and if their full significance is not appreciated, they may eventually become part of the clinical picture of infantile atrophy.

32. Talbot, F. B.: Casein Curds in Infants' Stools. Biological Proof of Their Casein Origin, Arch. Pediat., June, 1910.

33. Talbot: The Composition of Large Curds in Infants' Stools, Boston Med. and Surg. Jour., June 11, 1908.

Fat stools are very bright yellow (like Indian meal), oily and soft. They are composed of large amounts of fats, a good proportion of which is in the form of neutral fat or fatty acid. When one of these stools is placed on paper and then removed, there remains behind a grease-spot which will not absorb water (oiled paper). They are usually accompanied by very severe symptoms. Fat should be removed entirely from the milk for a time and very frequently these babies cannot be saved without human milk.

METABOLISM

Most of the figures offered us by metabolism experiments are obtained by the Rosenfeld method of extracting fat, and very recently by the Kumagawa and Suto method. These and other modern methods of fat extraction have been given in more or less detail in the appendix of this paper. Despite the fact that the figures so obtained may not be absolutely correct, I believe that they are of great relative value and help to clear up many of the cases of perverted digestion. While they do not say the final word on the subject, they lead to a more intelligent grasp of the pathology of digestion. This paper does not pretend to consider the rôle of the intestinal flora in normal and abnormal digestion, but I believe that they are of great significance in certain conditions and that they will be found to influence metabolism. For example, Kendall[34] has shown that two factors are necessary for fermentation: a carbohydrate food, and fermentative bacteria; in like manner putrefaction cannot take place without protein plus putrefactive bacteria. Fermentative bacteria cannot act on protein, and putrefactive bacteria cannot act on carbohydrate. It is very difficult, therefore, to draw any conclusions in a subject which is complicated by so many factors. The problems of digestion depend on the balance of all the factors concerned and when the normal balance is upset by any one or many factors, we have a pathologic condition.

The significance of fatty acids and soaps is as yet unknown; probably they are of very little significance in the questions of absorption. Freund (quoted above) has shown that an acid dyspeptic stool can be changed in many instances to a formed "soap stool" by a relative increase in the amount of casein, while an alkaline soap stool can be changed into an acid stool by a relative increase in the amount of carbohydrates. Coincident with the change from an acid to an alkaline stool (according to Kendall) there is a change of the intestinal flora; the acid-forming bacteria which previously predominated are replaced by the putrefactive group of bacteria. When an alkaline stool is made acid the reverse takes

34. Kendall: Boston Med. and Surg. Jour., 1911, clxiv (to appear in March). Read before Suffolk District Medical Society.

place. Bahrdt[35] has recently shown that babies passing "soap stools" have diminished powers of absorption and that they lose more fat than was formerly taught. He found the absorption of fat (Kumagawa and Suto method) as follows:

Name of Baby.	Age, Months.	Weight, Gm.	Fat absorbed. Per cent.	Character of Stools.
Schröder, 7 days	9	7470	82.4	Soap stools
Schüler, 7 days	2	3945	83.2	Mostly soap stools
Weiss, Ia, 5 days....	9/10	3750	81.9	Soap stool
Weiss, Ib	9/10	3750	86.0	Soap stool
Weiss II, 8 days.....	10	3900	93.0	Normal stools

Breast and skim milk.

The fat absorption in these babies with soap stools is, therefore, considerably less than that of normal infants. There is, however, not such a loss of fat as in diarrhea. There is a loss of magnesium and calcium[36] in these soap stools and there is no loss of sodium and potassium. If the stools become acid and change into soft fatty curds there is no longer a loss of calcium and magnesium, but there is a loss of sodium and potassium. With this change comes an increased loss of fat from the body.[36] If this condition becomes more pronounced with diarrhea, there is a considerable loss of fat with the alkalies; the baby loses weight and takes on the appearance of "infantile atrophy."[37] Such babies can only be saved by human milk.[38]

Biedert[39] and Demme[40] designated severe chronic disturbances of digestion in which the stools contained very large amounts of fat as "fat diarrhea." The latter had one such case which came to autopsy and was found to have disease of the pancreas. Hecht[41] and Reuss[42] have reported cases of congenital obliteration of the bile-duct with normal pancreas, in which only one-half of the fat was split. I examined the stools

35. Bahrdt, H.: Untersuchungen über das Symptom der Seifenbildung und die Ausscheidung der Basen im Darm des Säuglings, Jahrb. f. Kinderh., 1910, lxxi, 249.

36. Meyer, L. F.: Jahrb. f. Kinderh., April, 1910, p. 379.

37. Finkelstein: Ueber Alimentäre Intoxikation III, Jahrb. f. Kinderh., 1908, lxviii, 521 and 692.

38. Finkelstein's so-called alimentary intoxication will not be considered in this paper because I believe that the majority of cases which clinically come under this category are not diseases of metabolism, but are bacterial infections of the gastro-intestinal canal, and that the physiologic powers of digestion are so lowered by the disease that the various food components are not digested.

39. Biedert: Jahrb. f. Kinderh., 1879, xiv, 336; ibid. 1888, xxviii, p. 21.

40. Demme: Jahrb. über die Tätigkeit des Jennerschen Kinderspitals in Berlin, 1874 and 1877; quoted from Hecht, Die Faeces des Säuglings, etc., p. 128.

41. Hecht: Die Faeces des Säuglings und Kindes, Berlin-Wien, 1910, p. 128.

42. Reuss: Case of Obliterated Bile Duct (congenital) Reported in Discussion, Jahrb. f. Kinderh., December, 1908, 729.

of a baby, the autopsy on which showed biliary cirrhosis[43] and a patent bile-duct, and found a similar type of stool.

Tuberculous peritonitis in babies is primarily a disease of the lymphatic system and when the mesenteric glands become caseous they form a dam beyond which the fat cannot pass. It has been shown earlier in this paper that part of the fat is normally carried by the lymphatics to the blood stream. If this road is blocked with tuberculous tissue, it is reasonable that some of the fat should be lost from the body. I have found large amounts of fat in the stools of such babies. Hecht believes that 80 per cent. of the fat in the stool should be split, and considers that great divergence from this amount means either trouble with the bile or pancreatic juice. He reports a seven months, premature baby which was only able to split 53 per cent. of the fat, and considers this to be due to weak action of the pancreatic fat-splitting enzyme, which presumably is not completely developed. Finizio[44] explains a large amount of fat in the stool of an 11-months-old baby with mumps by probable trouble in the pancreas.

Czerny[45] believes that babies with an exudative diathesis can be harmed by fat. He finds that an increase in the amount of fat in the food will bring eruptions out on the skin. Steinitz and Weigert[46] have apparently proved the correctness of this assumption by a metabolism experiment.

There is no doubt that large amounts of fat can do a great deal of harm to most babies. Such babies come under two classes—those which have a normal digestion and are unable to digest excessive amounts of fat, and those which have diminished powers of digestion and are unable to digest normal amounts of fat. So much attention has been paid to the few babies that are unable to digest fat that we are apt to forget that most babies can digest fat within reasonable limits. L. F. Meyer[47] has recently shown in Finkelstein's clinic that when fat is increased in the food of normal healthy babies there is no loss of fat, or salts from the body. This dispels, in a very convincing way, the false impression that normal babies are unable to digest fat. John Howland of New York showed in a recent investigation (not yet published) that a baby could be fed on large quantities of fat without symptoms of indigestion and without acidosis. In my experience, it has been safe to increase the

43. Morse, J. L.: Jaundice in the New-Born, Boston Med. and Surg. Jour., Feb. 24, 1910.

44. Finizio: A Case of Fat Diarrhea Following Mumps, Pediat., September, 1909; Rev. in Jahrb. f. Kinderh., 1910, lxxi, 205.

45. Czerny: Zur Kenntnis der exudative Diathese, Part 1, Monatschr. f. Kinderh., 1906, iv, 1; ibid. Part 2, 1908, vi, 1; ibid. Part 3, 1909, vii, 1.

46. Steinitz and Weigert: Monatsch. f. Kinderh., 1910, ix, 385.

47. Meyer, L. F.: Jahrb. f. Kinderh., April, 1910, p. 379.

percentage of fat gradually up to 4 per cent. in most normal babies whose digestive powers have not previously been lowered by gross errors in feeding or by infection, and that they develop normally without any of the signs or symptoms of fat indigestion so long as their hygiene is perfect and they have no intercurrent infection.

APPENDIX

METHODS OF ESTIMATION OF FAT IN FECES

There is no such thing as a theoretically perfect method of estimating fat in the feces. The methods employed may be grouped under two heads: 1. Extraction methods which attempt to obtain all the substances soluble in ether. 2. Saponification methods, in which the higher fatty acids are set free by saponification from the various combinations in which they occur, separated as far as possible from the other products of the action of alkali used, and weighed as fatty acids.

EXTRACTION METHODS

These methods estimate all the substances soluble in ether without considering what form the fat was in. The criterion in determining the value of the particular method under consideration has been the gross yield of substance soluble in ether. The method which has been taken as a standard in recent years is that of Rosenfeld, because it gave higher yields than other methods of substances soluble in ether. This method has been criticized because the substances weighed contain nitrogen and phosphorus and a low percentage of fatty acid. I used a modification of this method[48] as follows:

The feces are weighed, thoroughly mixed with 95 per cent. alcohol and dried at 43-45 C., transferred to a desiccator, and dried to constant weight. A weighed portion of the dried feces is placed in a paper capsule and boiled in absolute alcohol for one-half hour. The capsule is then transferred to a Soxhlet tube and extracted eighteen hours with chloroform. The combined absolute alcohol and chloroform extracts are evaporated to dryness, and the residue from each extracted with petroleum ether. The petroleum ether is then filtered and the filter paper thoroughly washed with warm petroleum ether until the wash ether shows no trace of fat, by evaporation on a watch glass. The filtrate is evaporated to constant weight. This weight is recorded as representing the quantity of neutral fat and fatty acid in the weighed portion of dry stool.

The dishes used for the evaporation of the alcohol and chloroform extracts from the first extraction are washed with hot 3 per cent. hydrochloric acid alcohol. The filter paper, used for filtering the petroleum ether in the first step, is added to the capsule from which the neutral fat and fatty acid have been extracted and boiled one-half hour under a reflux condenser in 3 per cent. hydrochloric alcohol to which the HCl alcohol washings from the dishes, mentioned in the first step, are added. Next, it is boiled one-half hour with absolute alcohol; the combined capsule and filter paper are then transferred to a Soxhlet tube and extracted for eighteen hours. The hydrochloric acid absolute alcohol and chloroform extracts are evaporated separately, the residue in each is taken up in petroleum ether and the combined petroleum ether extract is filtered. The filtrate is evaporated to constant weight; this represents soaps.

The neutral fat and fatty acids (the fat first weighed) are dissolved in equal parts of absolute alcohol and sulphuric ether and the acidity determined by titrating against decinormal alcoholic sodium hydrate solution, using phenolphthalein as an indicator.

Kumagawa and Suto[49] found that the solvent which gave the largest yield of substances soluble in ether was alcohol used near its boiling point in a continu-

48. Boston Med. and Surg. Jour., Jan. 11, 1908.

49. Kumagawa and Suto: Ein neues Verfahren zur quantitativen Bestimmung des Fettes und der unverseifbaren Substanzen im tierischen Material nebst der Kritik einiger gebräuchlichen Methoden, I, Biochem. Ztschr. 1908, viii, 212.

ous extraction apparatus. This explains why the Rosenfeld method and its modifications obtain higher yields of fat than other methods. The Rosenfeld method, however, is the best one yet devised to estimate the relative proportion of neutral fat, fatty acids and soaps.

Folin and Wentworth[50] criticize this method because they have observed that prolonged chloroform extraction brings away materials with a distinct fecal odor, and they say that the best method for extraction is that which takes out the smallest amount and not that which extracts the largest amount. They have devised a method which apparently has many advantages over the Rosenfeld method. It is briefly as follows:

One gram of very finely powdered feces is weighed into a fat-free paper capsule, placed in an extraction apparatus and boiled twenty hours with an ethereal hydrochloric acid solution. The ether is then distilled off and with it goes the hydrochloric acid. A low boiling petroleum ether (Ligroin) is added and allowed to stand over night. This solution is filtered the next day into a weighed beaker and dried at a temperature of 95 C. for five hours. It is then dried and weighed as neutral fat and fatty acids. The next step is a new departure in chemistry, according to Folin and Wentworth, and is very important. The fat is dissolved in benzol, .5 per cent. alcoholic phenolphthalein added and it is heated almost to boiling. It is then immediately titrated against N/10 sodium alcoholate (made by dissolving 2.3 gm. metallic sodium in one liter absolute alcohol and standardized); 1 c.c. of this=28.4 m.gm. stearic acid. This method of titration undoubtedly has a great advantage over all that have been devised thus far.

SAPONIFICATION METHOD

Lieberman-Szekely described a method of determining the fat in the stool by first saponifying it and then splitting with acid and extracting with ether. This extract was purified with petroleum ether. This method does not estimate the fat in the stool, but all the higher non-volatile fatty acids in various combinations; and according to Kumagawa-Suto the fat may be reckoned from this by multiplying by the factor 1.046.

Kumagawa and Suto's[49] method gives the highest results of all methods and has been controlled by very accurate and painstaking experiments. It is as follows:

Two to 5 gm. of powdered feces are mixed in a beaker with 25 c.c. 5 per cent. NaOH (20NaOH in 100 c.c.) and heated two hours over a water bath. The beaker should be covered with a watch glass during this process. During the saponification the mixture is stirred now and then with a glass rod. After about ten minutes the powder dissolves and there are small flocculi left behind. After about two hours, the solution is transferred, still hot, into a hermetically closed separating funnel with a capacity of 250 c.c. The beaker is washed two or three times with about 5 c.c. warm water. Next the solution is acidified with 30 c.c. 20 per cent. H_2SO_4. After cooling well 70 to 100 c.c. ether is added and shaken well. A precipitate remains between the layers of solution. The clear water is decanted after separation. Then the brown colored ether is carefully decanted into a beaker. The funnel with the precipitate is washed twice with ether; it is then dissolved and shaken again with 30 to 50 c.c. ether and to that is added the strongly acid water of the first shaking, and it is again well shaken. The reaction is then acid and the remaining fatty acid is dissolved in the ether. These ether extracts are united, evaporated and again taken up with absolute ether, filtered through asbestos and evaporated. This extract, which contains coloring matter, fatty acid, lactic acid and other components, is heated at 50 C. first and extracted with petroleum ether. If this solution is milky it is allowed to stand one hour and then filtered through asbestos, dried at 50 C. and weighed. More detail concerning this method may be obtained by referring to Kumagawa and Suto's original article in which there is a vast amount of experimental data and criticism of other methods. In it the bibliography concerning the extraction of

50. Folin and Wentworth: Determination of Fat and Fatty Acid, Jour. Biol. Chem., June, 1910.

fat from the animal tissue is very complete. These findings have been substantiated by Inaba.[51]

Bahrdt, Edelstein, Langstein and Welde[52] have used a new method for the quantitative estimation of the free volatile fatty acids in the feces. This method is based on a method by W. Steinkepf which used vacuum distillation and steam for extraction. The method in brief is as follows:

A weighed amount of fresh feces was distilled in a temperature of 60 C. for two hours, with steam drawn through on the one side by a vacuum on the other. The distillate is titrated against N/10 sodium hydrate, with phenolphthalein as an indicator. The amount of acid present is estimated in terms of decinormal acid. The temperature of the water bath during the whole distillation should be 60 C. Generally the distillation goes well if there are 600 to 900 c.c. distillate in one hour. The original article should be consulted for detail of the method and the apparatus necessary.

This brief description of the newer methods of fat and fatty acid extraction has been added so that those who have a desire to commence metabolism work on babies will be able to choose for themselves and go back to the original sources. I feel that the last word has not been said, and that it is necessary to extract all feces, both by the Kumagawa and Suto method, and by some modification of the Rosenfeld method. The method offered by Folin and Wentworth is still in the experimental stage and the writers are "now working to perfect it."

311 Beacon Street.

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51. Inaba: Biochem. Ztschr., 1908, viii, 352.

52. Bahrdt, Edelstein, Langstein and Welde: Untersuchung über die Pathogenese der Verdauungsstörungen im Säuglingsalter, Ztschr. f. Kinderh., 1910, i, No. 2, 139.

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THE BACTERIOLOGY OF THE BLOOD IN EARLY LIFE*

FRANK SPOONER CHURCHILL, M.D., and CHARLES P. CLARK, M.D.
CHICAGO

Medical literature is full of reports of the bacteriologic examinations of the blood in adults, and much valuable information has been obtained therefrom. Various infections have been studied in this way: typhoid, pneumonia, endocarditis, erysipelas, osteomyelitis, and many of the obscure febrile cases so frequently seen in our hospital wards. But while much work of this nature has been done among adults, we find comparatively few reports on this subject among infants and children. In scarlet fever alone have bacteriologic examinations of the blood been made to any extent.

Study of this infection by Jochmann,[1] Baginsky, Slavyk,[2] Hektoen[3] and others, has shown the presence of a streptococcus, apparently identical in its characteristics with the streptococcus erysipelatis. Thus, Jochmann, studying 161 cases of scarlet fever, found the streptococcus twenty-five times. All of these patients died, and Jochmann, from analysis of his own cases and those of other authors, comes to the conclusion that the presence of this organism in the blood in scarlet fever gives an almost fatal prognosis. Curiously enough, however, neither Jochmann nor Slavyk found the streptococcus in the foudroyant cases, also invariably fatal.

Aside from these studies on scarlet fever, reports on other infections in children are meager. Rotch and Low[4] report a series of thirty-six cases comprising a variety of infections, the greatest number of any single infection being typhoid (eight). They point out the scientific and practical value of taking blood cultures and urge a more widespread use of this method of investigation.

Delestre[5] examined the blood in forty cases, the patients ranging in age from a few days up to 4 years, all suffering from infections likely to prove fatal. Thirty-two of the forty died; eight recovered. Among the eight recoveries there was but one infant showing an organism in the blood, and this organism was the influenza bacillus. In the fatal cases, the blood obtained either during life or immediately after death, showed

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*From the Children's Memorial Hospital.

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1. Jochmann: Deutsch. Arch. f. klin. Med. 1903, lxxviii, 209. Ztschr. f. klin. Med. 1904, liv, 408.
2. Slavyk: Jahrb. f. Kinderh., liii, No. 5.
3. Hektoen: Jour. A. M. A., 1903, xl, 685.
4. Rotch and Low: Jour. Am. Med. Assn., 1907, xlviii, 185.
5. Delestre: Ann. d. gynéc. et obst., 1901, lv, 51.

organisms in twenty-two, in order of frequency as follows: streptococcus, staphylococcus, pneumococcus and colon bacillus.

Delestre also examined the blood from twenty-one premature infants; of these nineteen died, and fifteen of the fatal cases showed organisms in the blood, the order of frequency being as follows: streptococcus, colon bacillus, staphylococcus and pneumococcus. The author attributes this susceptibility of the newly-born to bacteremia, to the extensive absorbing surface in the lungs and intestines, and regards these tracts as the main points of entry of the bacteria, though the umbilicus, of course, is another vulnerable point. He gives few details in his cases, not stating either the clinical or anatomic diagnosis. The blood taken during life was obtained by an incision into the skin, and he believes his technic was so nearly aseptic that there was no danger of contamination.

Otten[6] reports a series of 250 cases of lobar pneumonia in children up to 15 years of age, with blood-cultures in seventy. He found the pneumococcus in nine of these seventy cases, 13 per cent.; of these nine, four patients recovered; five died.

The paucity of studies on this important subject in children is undoubtedly due to the difficulty of obtaining sufficient blood for examination from this class of patients. The veins of children are so small that it is extremely difficult to get into them. We have ourselves experienced this difficulty, and, besides the cases reported below, have made numerous but unsuccessful attempts to obtain the blood from other patients, chiefly infants and young children. Others apparently have had the same experience. Indeed, one author, studying a large series of infections of otitic origin among adults, "throws up the sponge" at the outset and says that no attempt is made to study children on account of the difficulty of carrying out the technic. But considering the frequency of obscure febrile infections among infants and children, it would seem that in such patients especially, systematic bacteriologic blood-examinations might be of great value; furthermore, in view of the future possibilities of antivaccine and antiserum treatment, accurate knowledge of disease is more than ever desirable; hence any method of investigation which promises to give us this accurate knowledge should be thoroughly tested, and, if prolific of results, systematically employed. It seems worth while, therefore, to report the following cases, even though small in number:

TECHNIC

Most of the cases have been studied at the Children's Memorial Hospital, a few each at the Cook County and Presbyterian hospitals, and to the attending physicians at these institutions we are much indebted for the material used.

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6. Otten: Jahrb. f. Kinderh., 1909, lxix, 568.

The blood has been obtained by the usual method, from the median basilic vein just above the elbow. In two cases of suspected typhoid it was obtained from the lobe of the ear, as recommended by Peabody. Various kinds of syringes have been used, but the Luer glass-syringe has been the most satisfactory. The blood thus obtained has been mixed immediately at the bedside with various media: in most of the cases two tubes of bouillon, two of agar and agar plate have been inoculated. In five of the typhoid cases, ox-bile has been used as the medium, with positive results in all. A case of suspected typhoid in which bile medium was used was negative, but proved later to be a case of tuberculous meningitis.

In using the ox-bile as a medium, the following technic was observed:

Test tubes containing fresh ox-gall sterilized in the autoclave were used. The blood obtained from the vein, or from the lobe of the ear in some cases, was introduced directly into the test-tube of bile. This was then put in the incubator from fifteen to eighteen hours, at the end of which time a few loopfuls were transferred to a tube of coagulated blood-serum: after three to five hours of incubation microscopic examination of the water of condensation showed, in the positive cases, the presence of motile bacilli. The presence of such motile bacilli is now accepted as evidence of a typhoid or a paratyphoid organism.

We have made sixty-nine examinations on sixty-four infants and children during life, and have studied sixteen cases post mortem. It is with the former group of cases that we are chiefly concerned. This is composed of the following infections:

Disease	No of Cases	Results
Typhoid	20	11 Positive
Pneumonia—		
Lobar	15	3 Positive
Lobular	3	1 Positive
Rheumatism	5	5 Negative
Meningitis—		
Meningococcus	5	2 Positive
Staphylococcus	1	1 Negative
Tuberculous	1	1 Negative
Chorea	2	2 Negative
Pyelitis	2	2 Negative
Nephritis	1	1 Negative
Erysipelas	1	1 Negative
Appendicitis, General peritonitis and lobar pneumonia	1	1 Negative
Leukemia	1	1 Positive
General septicemia	1	1 Positive

In addition to the above one case each of scorbutus, miliary tuberculosis, arthritis deformans, toxic erythema and of tuberculous adenitis, gave negative results. Thus, of the sixty-nine examinations made on these sixty-four children, we have obtained nineteen positive results. These will now be analyzed according to individual infections.

TYPHOID

It is in this infection perhaps that the greatest amount of blood-culture work has been done among adults, with interesting and important results. During the first week of the disease, 95 to 100 per cent. of the patients will show the presence of typhoid bacilli in the circulating blood: with the progress of the disease, this number diminishes so that in the second or third week they are found much less frequently (40 per cent.). As the Widal reaction pursues exactly the reverse course, absent at first, present later, the blood culture test becomes an extremely important method in the early diagnosis of typhoid, at least among adults.

How is it among children? Our own cases are of course too few to warrant conclusions. We can state only that eleven of the twenty cases gave positive results, and that these positive results were obtained as early as the sixth and as late as the twenty-second day (Table 1). The negative results were obtained in the first case on the tenth, thirteenth and twentieth days, in the second case during the seventh week (relapse), and in the third and fourth cases on the eighth day.

Combining Rotch's series, our own and a few scattering reports in literature, we find thirty-one cases of typhoid fever, in twenty, or 66 per cent. of which, bacilli were found in the circulating blood. We find, furthermore, that they were found as early as four days before the onset of symptoms and as late as the twenty-second day. The former case was that of a 12-year-old child whose sister was already ill with typhoid (Conradi).[7]

These results were obtained with all kinds of media and at all periods of the disease. It is probable that with the more widespread use of Conradi's ox-bile medium and more frequent examinations early in the disease, this proportion of positive results will be considerably increased. Only when large numbers of cases have been examined, and at different periods of the disease, can we draw final conclusions as to the importance of this particular laboratory investigation. If the results of the future correspond with the results already obtained in large numbers of adults, this method will become even more valuable among children on account of the more irregular, atypical nature of the disease in early life. We urge a constant, widespread use of the method, that our knowledge in this direction may be increased as rapidly as possible.

PNEUMONIA

The pneumococcus is a frequent invader of the blood in adults, not only in pneumonia, but also in pneumococcic infections with the pathologic seat of the disease in other localities, e. g., the endocardium and pericardium, the joints, the meninges, the tonsils, etc. As in typhoid the literature is voluminous as to adults, meager as to children.

7. Conradi: Deutsch. med. Wchnschr., 1906, xxxii, 58.

Otten studied 250 cases of pneumonia in children up to 15 years of age. He made blood-cultures on seventy of these patients, finding the pneumococcus in nine, or 13 per cent. Of these nine children four recovered, five died.

Spitta[8] describes a case of lobar pneumonia in a 17 months' infant, with a general pneumococcic infection, resulting in an arthritis and empyema; pneumococci were found in the blood during the sixth week of illness and one week before death. Autopsy confirmed the antemortem examinations.

We have taken cultures in fifteen cases of lobar pneumonia and three of lobular pneumonia. Four of the cases in the former group were positive, one in the latter, the organism found being the pneumococcus in every instance.

Thus in the eighty-five cases comprising our own and Otten's series, thirteen, or 15 per cent., showed pneumococci in the circulating blood, a striking difference from its frequency among similar infections in adults. This failure to discover the organism more frequently in the blood in children is due to one of the two causes. Either the technic employed in the cases already studied is faulty, or the organism does not invade the blood frequently. The technic employed is apparently important, great discrepancies existing among the authors who have studied this question in adults. Thus Lenhartz, Schottmüller, Grimm and Jochmann find pneumococci in the blood in only one-fourth to two-thirds of their cases, whereas Procharska and Weins find them in practically *all* of their cases. The former group of observers worked with solid media—blood-agar; the latter with fluid media—blood bouillon.

To this difference in culture media, Otten attributes the varying results obtained by these workers, maintaining that the pneumococcus grows better on fluid media, and that consequently those who use such media will get a comparatively high percentage of positive results. He himself in his work on children used fluid media, yet got positive results in only 13 per cent. of his cases. Consequently, if his reasoning be correct, the pneumococcus is not a frequent invader of the blood in the lobar pneumonia of children. However, here again the cases available for study are too few to warrant final conclusions, either as to the frequency of its appearance or as to its prognostic value when present. Future investigations must determine these points.

THE RHEUMATIC AFFECTIONS

In this group we have included cases of endocarditis, arthritis, tonsillitis and chorea, these manifestations occurring either singly or in combination with each other (Table 1).

8. Spitta: Brit. Med. Jour., 1902, ii, 1579.

TABLE 1.—BACTERIOLOGY OF BLOOD ANTE-MORTEM

Case, Sex and Age	Clinical Diagnosis	Day of Disease	Number of Cultures	Medium	Result	Remarks
1—M.— 4 years.	Typhoid	?	1	.....	Negative..	Three Widal's incomplete; persistent leukopenia; recovery.
2—M.— 7 years.	Typhoid	10-13-20th day.	3	Agar plate; two bouillon.	All negative.	Recovery; Widal positive tenth day.
3—M.—12 years.	Typhoid	14th day.	1	Bile	Positive..	Recovery; Widal positive.
4—F.—11 years.	Typhoid	6th day.	1	Bile	Positive..	Recovery; Widal negative fourth day; culture taken second day of measles.
5—M.—42 months.	Typhoid	7th day.?	1	Bile	Positive..	Entered hospital for genu valgum; blood from ear third day of a measles rash; Widal negative sixth day.
6—F.— 5 years.	Typhoid	22d day.	1	Bile	Positive..	Recovery; Widal negative twenty-first day.
7—F.—10 years.	Typhoid	?	1	Bile	Positive..	.....
8—F.—11 years.	Typhoid	10th day.	1	.....	Positive..	Recovery; severe case; hemorrhages.
9—M.— 6 years.	Typhoid	7th week.	1	.....	Negative..	Negative during relapse; recovery; Widal positive eighth day.
10—F.— 8 years.	Typhoid	14-18th day.	2	.....	Both positive.	Recovery; Widal positive fifteenth day.
11—M.— 5 years.	Typhoid	6th day.	1	.....	Positive..	Recovery; Widal positive fifth day.
12—M.—12 years.	Typhoid	8th day.	1	.....	Negative..	Recovery; Widal positive eighth day; serum reaction to "paracolon" *B.* and "paratyphoid" *B.* negative.
13—M.—11 years.	Typhoid	3d week.	1	.....	Positive..	.....
14—M.— 4 years.	Typhoid	15th day.	1	.....	Negative..	Widal negative fifteenth and seventeenth days.
15—M.—42 months.	Typhoid	8th day.	1	.....	Negative..	Widal positive eighth day.
16—M.— 6 years.	Typhoid	7-12th day.	2	.....	Negative.. Positive..	Widal positive; recovery.
17—F.— 8 years.	Typhoid	9th day.	1	.....	Positive..	Widal positive; recovery.
18—F.— 8 years.	Typhoid	6th day.	1	.....	Positive..	Widal positive; recovery.
19—M.—10 years.	Typhoid	10th day.	1	.....	Negative..	Widal positive; recovery.
20—F.—10 years.	Typhoid	15th day.	1	.....	Negative..	Widal positive; death.
21—M.—18 months.	Pneumonia	?	1	.....	Negative..	Second day of a high temperature probably a relapse; outcome unknown; child removed from hospital against advice.
22—M.—30 months.	Pneumonia	?	1	.....	Negative..	Recovery.
23—M.— 7 years.	Pneumonia	15th day.	1	.....	Negative..	Lysis on fifteenth to sixteenth day; recovery.
24—M.— 9 years.	Pneumonia	10th day.?	1	.....	Negative..	Appendicitis; general peritonitis; pneumonia; death.
25—F.— 2 years.	Pneumonia	8th day.	1	.....	Positive..	Rachitis; temperature normal ninth day; convalescence tedious; recovery in two months.
26—M.— 3 years.	Pneumonia	8th day.	1	.....	Negative..	Crisis on ninth day; recovery.
27—M.— 2 years.	Pneumonia	4th day.	1	.....	Negative..	Cretin; death four hours after culture.
28—M.— 5 years.	Lobarpneumonia.	5th day.	1	.....	Positive..	Brother and sister on same day; pneumococci in sputum of each.
29—F.— 7 years.	Lobarpneumonia.	4th day.	1	.....	Positive..	
30—M.— 9 years.	Lobarpneumonia.	9th day.	1	.....	Negative..	Recovery.
31—M.—18 months.	Lobarpneumonia.	4th day.	1	.....	Positive..	Recovery.
32—F.— 6 years.	Lobarpneumonia.	7th day.	1	.....	Negative..	Recovery.
33—F.— 9 years.	Lobarpneumonia.	4th day.	1	.....	Negative..	Recovery.
34—M.—11 years.	Lobarpneumonia.	4th day.	1	.....	Negative..	Recovery.
35—F.—12 years.	Lobarpneumonia.	9th day.	1	.....	Negative..	Chronic endocarditis; recovery from pneumonia.
36—M.— 1 year.	Lobular pneumonia.	10th day.	1	.....	Negative..	Recovery.

37—F.—16 months.	Lobular pneumonia.	2d week.?	1	.....	Negative..	
	Lobular pneumonia.	Weeks.	1	.....	Positive..	Pneumococci in blood.
38—M.—20 months.	Empyema	?	1	.....	Negative..	Death.
39—F.—54 months.	Pulmonary abscess.	17 ?	1	.....	Positive..	Streptococci in blood and in pus from abscess; removed from hospital.
40—F.—11 years.	Chronic endocarditis	?	1	Blood agar; bouillon.	Negative..	Acute exacerbation; culture taken two months before death, May 1.
41—M.— 4 years.	Chronic endocarditis.	3d-11th day.	2	.....	Negative..	During intercurrent tonsillitis (streptococcus).
42—F.— 6 years.	Chronic endocarditis.	?	1	.....	Negative..	Culture second day of a three days' temperature; no evident cause; recovery from this.
43—M.—11 years.	Chronic endocarditis.	Months.	1	Agar bouillon....	Negative..	Antecedent history of rheumatism; entered C. M. H. 3-19-10; temperature, 98-103 from 3-27-10 to 4-7-10; culture taken 4-1-10; temperature 99-102 that day.
44—F.—11 years.	Chorea; chronic endocarditis.	7th week.	1	Agar bouillon....	Negative..	No elevation of temperature; recovery.
45—M.—10 years.	Chorea; chronic endocarditis.	19th day.	1	.....	Negative..	Antecedent rheumatism; culture taken after three-four days' temperature without evident cause, when it became normal.
46—F.—66 months.	Rheumatic fever.	9-16th day.	2	.....	Negative..	Chronic (?) endocarditis and arthritis; improvement, then measles, acute tonsillitis (streptococcus and staphylococcus), general septicemia; death; cultures during acute arthritis, etc.
47—M.— 3 years.	Meningitis	5th day.	1	.....	Negative..	Meningococcus in spinal fluid; death one month later.
48—M.—10 years.	Meningitis	?	1	.....	Positive..	Meningococcus in spinal fluid; death eleventh day.
49—M.—66 months.	Meningitis	7th day.	1	.....	Negative..	Meningococcus in spinal fluid; death fifty-first day.
50—M.— 9 years.	Meningitis	5th day.	1	.....	Positive..	Meningococcus in spinal fluid; recovery.
51—F.— 6 years.	Meningitis	48th day.	1	Bouillon; agar plate.	Negative..	Meningococcus in spinal fluid; death four weeks later.
52—F.—22 months.	Meningitis	12th day.	1	.....	Negative..	Staphylococcus in spinal fluid; recovery.
53—F.—10 years.	Meningitis	10th day.	1	Bile	Negative..	Suspected typhoid; Widal negative; von Pirquet positive tenth day; spl. fl. that of tuberculous meningitis; death.
54—F.—20 months.	Pyelitis	Weeks.	.....	.....	Negative..	Rachitis, chronic endocarditis, otitis media two days before culture; pneumonia six weeks later; death.
55—F.—18 months.	Pyelitis	8th day.	1	.....	Negative..	Recovery.
56—F.— 8 years.	Erysipelas	5th day.	.....	.....	Negative..	Recovery.
57—F.—12 years.	Acute nephritis..	4th day.	1	Agar bouillon...	Negative..	Entered C. M. H. with typhoid symptoms; Widal negative fourth day; leukocytes 18,000; culture April 8, 1910; endocardial murmur April 11 and pericardial friction-rub April 12.
		25th day.	1	.....	Negative..	Acute arthritis fifth day of fever; chorea.
58—F.—10 years.	Scorbutus.....	8th day.	1	.....	Negative..	Recovery.
59—M.—30 months.	Miliary Tb?	?	1	.....	Negative..	Positive Wassermann but no characteristic signs of syphilis; left hospital unimproved.
60—F.— 5 years.	Arthritis deformans.	?	1	.....	Negative..	Positive Wassermann; improving.
61—F.— 3 years.	Toxic erythema..	5th day.	1	.....	Negative..	Recovery; rachitis.
62—F.—15 months.	Tuberculous adenitis (cervical)	?	1	.....	?	.....
63—M.— 4 years.	Leukemia (lymphocytic)	Weeks.	1	.....	Positive..	Streptococci in blood one week before death.

Post-mortem examinations in cases of endocarditis have shown a varied bacteriology, streptococci, staphylococci, pneumococci, gonococci, pyocyaneus and influenza bacillus, all having been found in the heart's blood and on the valves of the heart in such patients. During life, in cases of septic endocarditis in adults, bacteria have often been found in the blood (Billings). We know practically nothing of this aspect of the subject in children, however. Our own group comprises seven cases; all had chronic endocarditis; in five of the cases, the cultures were taken during a febrile stage, due either to a tonsillitis, an arthritis, or to an unknown cause, possibly an acute exacerbation of the chronic endocarditis. There were two cases of chorea, and in both of these the temperature was normal when the cultures were taken. Cultures were negative in all seven of the cases.

MENINGITIS

It was formerly thought that in epidemic meningitis the meningococcus rarely invaded the blood, but recent investigations with improved technic show its presence in the blood in about 25 per cent. of the cases. We have examined four cases, with two positive results. In the tuberculous case the patient was examined on the tenth day of the disease as a suspected typhoid.

OTHER DISEASES

One case each of pyelitis, erysipelas and acute nephritis gave negative blood-cultures. Catheterized specimens of urine from the cases of pyelitis and nephritis showed a streptococcus in the former and nothing in the latter. One case of acute lymphocytic leukemia showed the streptococcus in the blood one week before death.

POST MORTEM

Much more work has been done on the bacteriology of the blood on children post mortem than ante mortem. After death the blood often shows the presence of organisms in great variety. We have reports on the bacteriology of the heart's blood in seventeen cases, of which thirteen showed positive results. These cases comprised the usual run of hospital patients: intestinal, pulmonary, bronchial, otitic, etc. (Table 2). Three cases of special interest were, one each of hemorrhagic disease of the newly born, erysipelas and status lymphaticus. The hemorrhagic disease showed in the heart's blood the *Staphylococcus aureus,* the bacillus coli, the streptococcus and an unidentified diplococcus midway between the pneumococcus and the streptococcus.

Of the four cases with a sterile heart's blood, three were as follows: A pyelo-nephritis due to the *B. pyocyaneus,* an otitis with a general septicemia, but with entirely negative post-mortem results, and a meningo-

TABLE 2.—BACTERIOLOGY OF BLOOD POST-MORTEM

Case, Sex and Age	Clinical Diagnosis	Anatomical Diagnosis	Blood		Hours After Death	Remarks
			Ante-Mortem	Post-Mortem		
1—..—12 days.	Hem. disease of newborn.	Septic thrombosis of umbilical vessels; numerous hemorrhages; meningitis	No examination.	Staphylococcus aureus coli; few streptococcus.	5	All organisms in cerebrospinal and peritoneal fluids; staphylococcus and B. coli only in pericardial fluid.
2—F.— 8 months.	Ileocolitis	Ileocolitis; bronchopneumonia.	No examination.	Streptococcus	3	Streptococcus in pericardial pleura, peritoneal and splenic fluid; staphylococcus aureus in bile, splenic and pericardial fluids.
3—M.— Infant.	Rachitis	Enterocolitis; rachitic osteochondritis.	No examination.	Smears: Gram-positive coccus and a gram-negative bacillus. Cultures: Staphylococcus aureus and colon bacillus.	8	.....
4—M.— 4 months.	Malnutrition ...	Ileocolitis; bronchopneumonia.	No examination.	Three organisms resembling in all respects streptococcus pyogenes, staphylococcus aureus and diplococcus lanceolatus.	6	Some organisms from pus of lung.
5—F.— 4 months.	Gastro-enteritis..	Gastro-enteritis; otitis media; bronchitis; meningitis.	No examination.	Negative	36	Cultures from cerebrospinal fluid showed the colon bacillus.
6—M.— 3 months.	Bronchopneumonia	Bronchopneumonia; bronchiolitis; cerebrospinal meningitis; patent ductus arteriosus.	No examination.	Staphylococcus aureus; streptococcus pyogenes.	28	Cultures from cerebrospinal fluid showed: diplococcus lanceolatus, staphylococcus aureus, streptococcus pyogenes, *B.* fecalis alk.
7—M.— 6 months.	Enterocolitis*...	Enterocolitis	No examination.	Staphylococcus albus	30	.....
8—F.—11 years.	Endocarditis....	.....	Negative.	Negative	16	Bouillon only used post-mortem.
9—F.— 3 years.	Otitis; general septicemia.	Nothing abnormal found.	No examination.	Negative	16	.....
10—M.—14 months.	Pyelonephritis...	Pyelonephritis; bronchopneumonia, cloudy swelling of myocardium, liver and kidney.	No examination.	Negative	18	*B.* pyocyaneus in pelvis of left kidney; also *B.* coli; staphylococcus albus from mesenteric gland; staphylococcus aureus from right ureter; staphylococcus citreus and micrococcus tetragenus from pericardium.
11—F.— 5 months.	Enterocolitis....	Enterocolitis	No examination.	Staphylococcus albus	50	.....
12—F.—18 months.	Meningitis	Status lymphaticus.	No examination.	A diplococcus midway between the pneumococcus and the streptococcus pyogenes; colon bacillus; streptococcus.	1	No meningitis.
13—F.—20 months.	Rachitis; pyelitis; endocarditis; laryngitis; lobarpneumonia	Rachitis; acute nephritis; vegetative endocarditis; laryngitis; lobar pneumonia.	Negative.	Contamination ?	..	Colon bacillus on trachea. (Case 56, Table 1.)
14—M.— 3 months.	Enterocolitis ... Erysipelas	.....	No examination.	Streptococcus	..	.....
15—..— 3 months.	Lobarpneumonia	Pulmonary tuberculosis.	No examination.	Streptococcus	15	.....
16—F.— 6 months.	Meningitis (meningococcus).	Purulent meningitis.	No examination.	Negative	..	Meningococci in spinal fluid, antemortem.
17—M.—	Infant atrophy..	Lobular pneumonia; patent foramen ovale.	No examination.	Negative	24	.....

* Case 26, Table 1.

coccic meningitis. The fourth case was an endocarditis in which the antemortem blood was also sterile (Case 26, Table 2).

The organisms recovered post mortem were as follows: the staphylococcus six times, aureus five times, albus one time, the streptococcus eight times, bacillus coli three times, the *Diplococcus lanceolatus* one time, and the unidentified diplococcus already mentioned.

We are much indebted to Prof. E. R. LeCount of the Pathological Department of Rush Medical College, under whose supervision most of the post-mortem work in our cases was done.

SUMMARY

The main points in this paper may be briefly summarized as follows:

Blood-cultures in adults during life, in large numbers of cases, have yielded information of scientific interest and diagnostic value.

Little work in this direction has been done in the infections of early life. There is need of more of this work among infants and children.

It is reasonable to suppose that blood-cultures in early life may be of even more value than in adult life, on account of the greater frequency of obscure infections during the former period.

1259 North State Street.

THE METABOLISM OF NITROGEN, PHOSPHORUS AND THE PURIN SUBSTANCES IN THE NEW-BORN; WITH SPECIAL REFERENCE TO THE CAUSATION OF THE URIC ACID INFARCTS OF THE KIDNEY *

OSCAR M. SCHLOSS, M.D., AND JAMES L. CRAWFORD, M.D.
NEW YORK TROY, TEXAS

I. INTRODUCTION

During the first few days in the life of an infant a number of phenomena may occur which border closely on the pathologic, among which is the frequent, if not constant, deposit of uric acid or its salts in the kidney tubules. Numerous investigations have been directed toward the solution of the etiology of this condition, in spite of which a number of the factors concerned are still obscure. Our own investigation was undertaken in the effort to determine the uric acid output, the factors on which it depends, and certain related problems of metabolism in the new-born infant.

It is a common observation that the urine of the new-born is often turbid and frequently leaves a deposit of uric acid or urates on the napkin; and in a large percentage of the infants who die during the first few days of life, a deposit of uric acid or urates[1] is found in the medullary portion of the kidney—the so-called uric acid infarcts. It has been observed that these deposits are rarely present in dead-born infants; that they are found with greatest frequency in infants dying between the second and eighth days of life, and that their occurrence is infrequent after the twentieth day.

In 282 autopsies on living-born infants collected by Hodann,[2] infarcts were present in 117 cases (42 per cent.). Hecker[3] noted their presence in 40 per cent. of infants who had lived from a few hours to two months. Salomenson's[4] statistics show their presence in 39 per cent. of 462 living-born infants.

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* From the Laboratory of Biological Chemistry of Columbia University at the College of Physicians and Surgeons, New York, and the New York Nursery and Child's Hospital.

1. Reusing and Ebstein considered that the uric acid was deposited as such. Parrot and Salomenson believed that it occurred as sodium urate, while Flensberg and Virchow thought that the infarct salt was ammonium urate. The analysis of Sjöqvist indicates that the uric acid is deposited as acid ammonium urate, or perhaps a mixture of this salt and neutral ammonium urate.

2. Quoted by Czerny and Keller: Des Kindes Ernährung, Ernährungsstörungen, etc., 1906, p. 167, etc.

3. Hecker: Virchow's Arch. f. path. Anat., 1857, xi, 217.

4. Salomenson: Quoted by Flensberg.

It was shown by Martin and Ruge,[5] Parrot and Robin,[6] Virchow,[7] Hofmeier,[8] Ebstein,[9] Flensberg[10] and others that the infarct elements—hyaline or granular cylinders or spheres incrusted with uric acid or urates—are frequently present in the urine of the new-born and are identical with those found in the kidney. In sixty-three observations on infants from birth to 8 days of age by Hofmeier, these elements were found in 62 per cent.[11] In the reports collected by Flensberg, their presence was noted for the urines of 101 (58 per cent.) of 173 infants from birth to the sixth day of life. They were present in nearly 90 per cent. of the cases in which the urine was examined during the last half of the first day and during the second day of life. The results were positive in all of the twenty infants examined by Flensberg. These results led Flensberg to believe that the causation of such infarcts is a physiologic processs and occurs to some degree in all new-born infants.

A great number of hypotheses have been advanced to explain the causation of the infarcts. Schlossberger[12] considered that intestinal disturbances gave rise to an increased excretion of uric acid, and that a sedimentation of the urine was induced by a contraction of the urinary tubules, due to a low body temperature. Virchow[7] attributed their occurrence to the revolution of metabolism which occurred at birth. Miller[13] sought their explanation in a low temperature, insufficient respiration and oxidation, and renal congestion due to increased work thrown on the heart. Vierordt[14] considered that the feeble powers of oxidation, and the concentration of the urine due to the small fluid intake, were the important factors. Coming to the more specific explanations we have that of Ebstein[9] who thought that there was a primary deposit of uric acid which caused a necrosis of the kidney parenchyma, and thus gave rise to the infarct stroma. The uric acid excretion in the new-born was determined by Reusing[15] who found that it was very high. He considered that this high uric acid output, and the high acidity of the urine were the predisposing factors; the exciting cause was the great concentration of the urine due to the deficient fluid intake. Sjöqvist[16] deter-

5. Martin and Ruge: Ztschr. f. Geburtsh. u. Frauenkr., 1876, i, 273.
6. Parrot and Robin: Arch. gén. de méd., 1876, i, 129, 309.
7. Virchow: Gesammelte Abhandlungen zur wissensch. Med., 1856, p. 833.
8. Hofmeier: Virchows Arch. f. path. Anat., 1882, lxxxix, 493.
9. Ebstein: Die Natur und Behandlung der Harnsteine, Wiesbaden, 1884.
10. Flensberg: Nörd. Med. Ark., 1894, No. 9, N. S.; Centralbl. f. inn. Med., 1894, xv, 965.
11. Hofmeier found the infarcts in a much larger percentage of infants whose mothers had been chloroformed during labor.
12. Schlossberger: Quoted by Czerny and Keller, p. 160.
13. Miller: Jahrb. f. Kinderh., 1886, xxv, 187.
14. Vierordt: Gerhardt's Handbuch der Kinderkrankheiten, 1877, i, 147.
15. Reusing: Ztschr. f. Geburtsh. u. Gynäk., 1895, xxxiii, 36.
16. Sjöqvist: Nörd. Med. Ark., 1894, No. 10, N. S.; Maly's Jahresb., 1894, xxiii, 245.

mined the uric acid in catheterized specimens of urine obtained by Flensberg, and found that there was a great increase during the infarct period—the last half of the first day and the second day of life. Flensberg[10] considered that the exciting cause of the infarcts was the excretion of an albuminous material into the tubuli contorti during fetal life and shortly after birth. The casts which formed the groundwork for the infarcts were thus developed, and, coming in contact with the concentrated urine, received a deposit of uric acid.

The problem of the etiology of this condition presents, therefore, two important phases for solution. First, the cause for the high uric acid output shown by Reusing and Sjöqvist, and next, the cause for the deposit of uric acid in the kidney tubules. It was toward the solution of the former that this investigation was especially directed.

II. EXPERIMENTAL

Technic.—Observations were conducted on nine full term, male infants who were nursed by their own mothers. Labor was normal in all cases. The mothers received only small amounts of chloroform; never enough to induce narcosis, and rarely more than 30 c.c. All of the infants were apparently normal at birth and remained so during the period of observation. Two of the infants showed a very mild degree of jaundice (Protocols IV and VI).

The urine was collected by means of a drawn out test-tube which was fastened over the well lubricated penis, and connected by means of glass and rubber tubing to a bottle attached to the side of the crib. Powdered thymol was used as a preservative. The glass tube was attached by means of wool knitting floss and adhesive plaster. The floss strands were arranged so as to encircle the body and thighs; the adhesive plaster was used to attach the glass tube to the floss bands. The method has the advantage that the adhesive plaster does not touch the delicate skin of the infant, thus avoiding all irritation; that it can be used in circumstances where restraint is not permitted; and that the apparatus needs no readjustment at the time of maternal nursing. It has the great disadvantage that part of the urine may be lost unless the infant is closely watched, and unless the body is elevated or the glass tube fastened to the napkin and set slantingly so that there is a gradual incline from the penis to the collecting bottle. To obviate this difficulty the infants were kept on their sides and the tube included in the portion of the napkin which passed around the lower thigh. As a further precaution, a layer of absorbent cotton was wrapped around the upper end of the glass tube so that any leakage of urine could be easily detected. Occasionally, edema of the prepuce developed, but in most instances it was slight and was due to insufficient lubrication of the penis, or the tube was fastened so tightly around the base of the penis that it interfered with the circulation. The edema usually subsided promptly on correction of the underlying fault.

but in two instances it was sufficiently severe to require removal of the apparatus before the conclusion of the experiment. The feces were collected by means of thin rubber napkins and were washed into a suitable receptacle with small quantities of distilled water.

The uric acid was determined by the method of Folin and Shaffer,[17] the acidity by the method of Folin,[18] the total nitrogen by the Kjeldahl process, and the purin content of the milk and feces by the method of Krüger and Schittenhelm.[19] Phosphorus was determined gravimetrically as magnesium pyrophosphate after oxidation by the method of Neumann.[20] The method for the purin bases varied depending on the amount of urine available. Either Kenneway's modification of the Cammerer-Arnstein method,[21] or the method of Krüger and Schmid[22] was used. In the latter the precipitation was made from an acid solution as advised by Benedict and Saki.[23] The specific gravity was determined with a small hydrometer standardized against distilled water.

The determinations were made in duplicate whenever the amount of material permitted, and all procedures were carefully checked. Blank nitrogen determinations were made with each series and the results deducted from the actual determinations. The leukocytes were counted by means of the Thoma-Zeiss apparatus and the counts were made at the same time each day—directly before a nursing.

As a matter of convenience the periods were taken from 9 a. m. to 9 a. m. The first day period varied, but extended from the time of birth to 9 a. m. the next day, when this period approximated twenty-four hours, and when the amount of urine was sufficient for examination. Otherwise, the period was extended another twenty-four hours. The exact time in each case is shown in the protocols.

The urine of the first few days often contained a sediment which it was necessary to dissolve before proceeding with the chemical examination. This was done by diluting with hot distilled water and adding, when necessary, a few drops of a 1 per cent. solution of sodium hydroxid.

It has been shown by Budin,[24] Rebemont,[25] Shücking,[26] Schiff,[27] Hofmeier[28] and others that the total blood mass of the new-born infant may be influenced to a considerable degree by the time of ligation of the umbil-

17. Folin: Am. Jour. Physiol., 1905, xiii, 49.
18. Folin: Am. Jour. Physiol., 1905, xiii, 53.
19. Krüger and Schittenhelm: Abderhalden's Handbuch der Biochemie, 1910, iii, 893.
20. Sherman: Organic Chemical Analysis, 1905.
21. Kenneway: Jour. Physiol., 1909, xxxix, 296.
22. Krüger and Schmid: Ztschr. f. physiol Chem., 1905, xlv, 1.
23. Benedict and Saki: Jour. Biol. Chem., 1909, vii, 27.
24. Budin: Quoted by Rebemont (see note 25).
25. Rebemont: Arch. de Tocologie, 1879, vi, 572.
26. Shücking: Berl. klin., Wchnschr., 1877, xiv, 5.
27. Schiff: Jahrb. f. Kinderh., 1892, xxxiv, 159: Ibid, 1893, xxxv, 21.
28. Hofmeier: Ztschr. f. Geburtsh. u. Gynäk., 1897, iv, 114.

ical cord. By various means, it has been determined that when the infant is left attached to the placenta some time after birth, it receives from 38 to 100 grams more blood than when the cord is ligated immediately after birth. According to Hofmeier the infant's blood mass may be thus increased by about one-third. Since it is only rational to suppose that there would be differences in the physiology of the new-born infant, dependent on the time of ligation of the umbilical cord, some of which have been shown by Hofmeier,[28] Schiff[27] and Reusing,[15] our cases have been divided into two series. In one series of four cases the umbilical cord was ligated immediately after birth, in the other five cases the infants were left in contact with the placenta for from two to five minutes after the pulsation of the cord had ceased.

Quantity and Physical Characteristics of the Urine.—The quantity of urine excreted, its relation to the fluid intake, and the specific gravity of the urine have been determined by a number of observers (Parrot and Robin,[6] Martin and Ruge,[5] Schiff,[27] Reusing,[15] Hofmeier,[28] Cruse[29] and others), and from much larger series of cases than we have had at our disposal. For this reason it is unnecessary to give detailed consideration to these characteristics. In conformity with the results of Hofmeier, Schiff and Reusing, the late ligation cases showed a greater urine excretion during the first few days than did the early ligation cases.

In all of our cases the appearance of the urine was noted, and the sediment, when present, or, in its absence, a centrifugalized specimen was examined microscopically. Epithelial cells and granular and hyaline casts were present in all cases at some time during the first four days. In all cases the urate spheres or uric acid cylinders were found at one time or another during the first three days. If the presence of the infarct elements in the urine signifies the occurrence of infarction—which there is no reason to doubt—our results agree with those of Flensberg, and indicate that the deposit of uric acid in the kidney is a regular occurrence in the new-born infant.

Uric Acid.—Reusing[15] determined the total uric acid elimination in the new-born by the method of Hopkins, and Sjöqvist,[16] the percentages by the Ludwig-Salkowski method. The uric acid values obtained by Reusing, Sjöqvist and those from our cases are shown in Table 1.

The values of Reusing are practically constant, with the exception of the increased excretion on the third day. Reusing explained this increase on the basis of the increased amount of urine excreted on this day, which was thus able to dissolve larger amounts of uric acid. Our values are higher than those of Reusing during the first four days; for the fifth, sixth and seventh days the average excretion was greater in Reusing's cases. A further and more important difference arises from the fact that while the average excretion in Reusing's cases was almost constant, with

29. Cruse: Jahrb. f. Kinderh., 1877, xi, 393.

the exception of the third day, ours showed a rapid increase during the second and third days and then a diminution.[30] The relatively high excretion of uric acid in infancy is readily seen when the values in Table 1 are compared with the adult values of 300 to 600 mg. of endogenous uric acid per day (Burian and Schur).

TABLE 1.—THE URIC ACID ELIMINATION IN THE NEW-BORN

	Average Daily Excretion of Uric Acid in Mg.	
Day.	Reusing, 6 Cases.	Schloss-Crawford, 8 Cases.
1	41.1	59.3
2	41.1	75.5
3	83.1	91.0
4	39.5	62.3
5	56.6	42.7
6	46.3	36.4
7	37.3	36.1
8	...	36.0
9	...	29.3

Sjöqvist.	Uric Acid per 100 c.c. Mg.
1. Mixed urine of 20 infants, first 12 hours of life.	82
2. Mixed urine of 20 infants during second half of first day and during the second day.	232
3. Mixed urine of 20 infants, 5 to 7 days old.	20.3
4. Mixed urine of 4 infants, 5, 6 and 7 days old.	10.4

The percentage determinations of Sjöqvist cannot be accurately compared with those of Reusing or ourselves, owing to the difference in the periods. His results, however, show a close relationship between the uric acid elimination and the occurrence of the infarcts. The uric acid was comparatively low before the infarct period, rose to a high level during the infarct period, and then sank to its lowest value. This relationship is also shown by our results when they are arbitrarily divided into three-day periods (Table 2).

TABLE 2.—THE URIC-ACID ELIMINATION DURING THREE-DAY PERIODS

Period.	Average Excretion of Uric Acid, Mg.
1. First, second and third days	75.2
2. Fourth, fifth and sixth days	47.1
3. Seventh, eighth and ninth days	33.8

Nieman[31] has determined the uric acid output in a new-born infant and the results are approximately the same as those in our cases. Nieman found, however, only a trace of uric acid during the first day, while the maximum excretion of 99.07 mg. occurred on the fourth day. After the fourth day the uric acid excretions in this case, and in two others—one

30. In the individual cases the uric-acid excretion varied rather widely, but was usually lower on the first than on the second or third day. This, however, is not without exception (Protocols VII and VIII). These variations are due, in part, at least, to the fact that our first-day period often consisted of more than twenty-four hours. From the end of the first day the numbered days were exactly twenty-four hours each, but owing to the variations in the first day, the later days as numbered in the protocols and tables do not always indicate the exact time from birth.

31. Nieman: Jahrb. f. Kinderh., 1910, lxxi, 286.

an infant of 6 days, the other of 8 days—were practically the same as those in our cases.

Orgler[32] determined the uric acid elimination in two breast-fed infants aged 11 days. The average daily excretion was 41.3 and 43.3 mg., respectively, which values are somewhat greater than those obtained by us for the urine of the ninth day.

In our cases there were certain differences in the uric acid output in the two series—the early and late ligations. These are shown in Table 3.

TABLE 3.—URIC-ACID EXCRETION IN THE IMMEDIATE AND LATE LIGATION CASES

	Uric Acid in Mg.			
	Average.		Per Kilo of Body Weight.	
Day.	Immediate Ligation (4 Cases).	Late Ligation (4 Cases).	Immediate Ligation (4 Cases).	Late Ligation (4 Cases).
1	60.7	57.8	16.7	16.4
2	57.5	89.0	15.8	26.7
3	82.3	102.6	24.0	30.9
4	64.0	60.0	18.3	18.2
5	44.9	40.3	12.7	12.1
6	36.8	36.6	10.	10.5
7	35.9	36.3	9.6	10.6
8	36.7	35.3	9.7	10.
9	29.2	29.4	8.4	9.6

The most important differences occur in the values for the second and third days. For these days the average uric acid excretion and the excretion per kilo of body weight was much greater in the late ligation cases. Throughout the period of observation, with the exception of the first, fourth and fifth days, the uric acid output per kilo was greater in the late ligation cases; but the differences after the third day are slight and are not decided enough to be of significance for such a small series of cases. The average excretion after the third day is greater for some days in the immediate ligations, for others in the late ligations, but the differences are too slight to offer conclusive evidence in favor of either series.

Reusing[15] observed that uric acid infarcts were less common in artificially fed infants than in those which had been nursed by their own mothers. This difference has been attributed to the greater urine excretion (from greater fluid ingestion) in the artificially fed. There is, however, another important difference. During the first two or three days of life the breast-fed infant receives colostrum which differs considerably from mature milk in both its physical and chemical characteristics. Milk is generally considered as practically purin free, and the uric acid excretion in infancy is in consequence entirely endogenous. But this applies only to the mature milk. When one considers the cellular content of colostrum as shown by microscopic examination, and the acute congestion of the breasts during the establishment of the milk secretion, it is only rational to suppose that colostrum contains an appreciable amount of

32. Orgler: Jahrb. f. Kinderh., 1908, lxvii, 383.

purin nitrogen. The results of our determinations in this connection are shown in the accompanying Table 4.

TABLE 4.—THE PURIN CONTENT OF COLOSTRUM AND THE MILK SECRETION OF THE FIRST ELEVEN DAYS

	Purin Nitrogen per 100 c.c. Mg.
Colostrum *	
1. Mixed specimen	3.9
2. Mixed specimen	2.99
3. Mixed specimen	3.37
4. Mixed specimen	4.07
5. Mixed specimen during acute congestion of breasts	5.73
6. Mixed specimen during acute congestion of breasts	5.9
7. Mixed specimen Case (protocol) IX, for first three days	4.7
Milk—Mixed Specimens—	
1. First and second days of true lactation	2.64
2. First and second days of true lactation	2.49
3. Third and fourth days of true lactation	1.69
4. Sixth and seventh days of true lactation	0.57
5. Seventh and eighth days of true lactation	0.92
6. Tenth and eleventh days of true lactation	0.9
7. Case (protocol) IX, fourth, fifth and sixth days	1.8
8. Case (protocol) IX, seventh, eighth and ninth days	0.8

* We wish to acknowledge our indebtedness to Dr. Wilbur Ward, Resident Physician at Sloan Maternity Hospital, for his kindness in obtaining Specimens 3 and 5.

These results show that colostrum contains an appreciable amount of purin nitrogen, which rises to its highest value during the acute congestion of the breasts, and then gradually falls. To determine what influence the purin nitrogen of colostrum might exert on the purin excretion in the new-born, we have determined the intake of colostrum in five cases by weighing the infant before and after each nursing. In four cases the purin nitrogen was calculated from the figures shown in Table 4. In Case 9 the purin nitrogen was determined in a composite specimen of milk obtained by pumping the mother's breasts before and after each nursing. In the first four cases the purin nitrogen was determined in the feces for the period, but in Case 9 the feces were not examined for purin nitrogen owing to their use for other purposes. The usual calculations for absorption give the results shown in Table 5.

TABLE 5.—CALCULATIONS FOR ABSORPTION OF PURIN NITROGEN

	Purin Nitrogen Ingested, Mg.	Purin Nitrogen in Feces, Mg.	Purin Nitrogen Absorbed, Mg.
Case 4	27.6	11.6	16.
Case 5	13.4	12.2	1.2
Case 6	18.3	15.3	3.
Case 7	23.1	18.3	4.8

Judging from these figures only a small amount of purin nitrogen is absorbed, and with the possible exception of Case 4, the quantity of uric acid from this source is negligible. A large proportion of the purin nitrogen in colostrum is probably bound in the nuclei of the colostrum corpuscles, epithelial cells and leukocytes. There is no proof that the new-born

infant is able to digest and absorb purin in these forms. There is, however, a great fallacy in the calculations for absorption. The stools of this period consist in part of meconium, which is formed in intrauterine life, and which contains a comparatively large amount of purin nitrogen. It was shown by Weintraud[33] and later by Schittenhelm[34] that meconium contains uric acid, which is probably derived from swallowed amniotic fluid. Meconium also contains epithelial cells which would serve as an additional source of purin nitrogen.[35] In our cases the first meconium stools were excluded and the feces collected after the appearance of yellowish or greenish particles, indicating a food residue. But this precaution does not eliminate the fallacy, for it is impossible to mark the exact time when the meconium stools cease and the food stools begin. Some meconium is frequently passed for from two to five days, depending on the amount of food taken.

We have no data to show that the "integral factor" of Burian and Schur—that one-half of the purin nitrogen ingested appears in the urine—applies to the new-born infant.[36] Assuming that this is the case, our calculations would be as shown in Table 6.

TABLE 6.—THE EXCRETION OF EXOGENOUS PURIN NITROGEN CALCULATED FROM THE PURIN NITROGEN INGESTED BY MEANS OF THE "INTEGRAL FACTOR"

	Purin Nitrogen Output During Colostral Period, Mg.	Calculated Exogenous Purin Nitrogen for the Period, Mg.
Case 4.....	90	13.8
Case 5.....	..	6.7
Case 6.....	77	9.1
Case 7.....	117	11.5
Case 9.....	94.9	5.9

The purin nitrogen ingested during the first three days can, therefore, explain but a small portion of the purin nitrogen excreted in the urine. The purin nitrogen excreted in the urine must be mainly, if not entirely, endogenous.

Purin Base Nitrogen.—The excretion of purin base nitrogen varied considerably in the individual cases but was usually most during the time of the greatest uric acid excretion. This is shown in Cases (Protocols) 1, 3, 4, 7, and 8. In Case (Protocol) 6, the amount of excreted purin base nitrogen was relatively small, while the uric acid elimination was greatest, and rose to its highest level when the uric acid was decreasing. It seems probable that the high purin base excretion and the high uric acid excretion of the former period were of the same origin, but for some

33. Weintraud: Centralbl. f. inn. Med., 1895, xvi, 433.

34. Schittenhelm: Deutsch. Arch. f. klin. Med., 1904, lxxxi, 423.

35. It is also true that a considerable portion of the purin nitrogen in the feces of adults does not originate from the food (Schittenhelm).

36. In experiments on infants more than 5 days of age, Nieman (see Note 31) found that the portion of the ingested purin nitrogen which was excreted in the urine was practically the same as in adults. It does not necessarily follow, however, that these experiments apply to the new-born infant.

unknown reason the excretion of the former was delayed. An indication of this delayed excretion is seen in Case (Protocol) 1, in which the highest uric acid and purin base values were not coincident. The purin bases showed only a slight increase at the time the uric acid was highest, but rose to their greatest values on the following days—times when the uric acid was decreasing. In Case (Protocol) 2 the excreted purin base nitrogen was comparatively small in amount during the entire period of observation, with the exception of a slight increase on the fourth day. The relation of the excretion of the purin bases to the uric acid excretion is shown in the new-born infant observed by Nieman;[31] there was a great increase in the purin base excretion when the uric acid values were increasing.

The average purin base excretion in our cases is shown in Table 7.

TABLE 7.—AVERAGE EXCRETION OF PURIN BASE NITROGEN (EIGHT CASES) *

Day.	Average Excretion in Mg. All Cases.	Average Excretion in Mg. for Immediate Ligations (4 Cases).	Average Excretion in Mg. for Late Ligations (4 Cases).
1	5.3	5.2	5.5
2	9.3	7.9	10.8
3	8.1	6.5	9.7
4	6.9	6.9	7.0
5	6.1	7.3	5.1
6	5.6	4.0	7.2
7	3.7	3.3	4.0
8	3.5	3.5	3.4

* It is possible that these average figures do not indicate the true average quantities of purin base nitrogen, since the same method of estimation was not used in all cases. The variation was necessitated by the different and at times small quantities of urine available for this examination. This applies especially to Cases 1 and 2, in which the purin base nitrogen was determined in small quantities of urine. The results of the daily determinations in Cases 3 and 4 and the determinations for three-day periods in Cases 6, 7 and 8, are comparable, since the same methods were employed, with the use of approximately the same amounts of material.

Leukocytosis.—Soon after birth there is a great increase in the number of leukocytes and later a pronounced decrease. This has been shown by Gundobin,[37] Schiff,[38] and others. The average leukocyte count in our cases is shown in Table 8.

These figures show the high leukocyte count, and later, the great decrease of the leukocytes, during the first three days of life. In most instances our data are based on a single daily estimation, and therefore do not show the rather frequent fluctuation of the leukocytes during the first days of life. We cannot lay much stress on the differences shown between the immediate and late ligation cases as indicating the usual

37. Gundobin: Jahrb. f. Kinderh., 1893, xxxv, 187.

38. Schiff: Ztschr. f. Heilk., Prague, 1890, xi, 17; Jahrb. f. Kinderh., 1892, xxxiv, 159.

conditions, for our series of cases is too small. Moreover, a single count each day is not sufficient for this purpose, but counts should be made at frequent intervals. Our results are merely intended to show the leukocyte count in the cases used in this investigation.

TABLE 8.—AVERAGE LEUKOCYTE COUNT FOR THE FIRST EIGHT DAYS (EIGHT CASES)

	Leukocytes per Cubic mm. of Blood.		
Day.	Average, All Cases.	Average, Immediate Ligations (4 Cases).	Average, Late Ligations (4 Cases).
1	29,000	28,600	29,400
2	16,800	17,900	15,700
3	11,800	13,700	9,900
4	10,300	10,800	9,800
5	10,600	10,200	11,100
6	11,700	11,100	12,300
7	12,000	10,200	13,900
8	11,600	11,300	12,000

Total Nitrogen.—The total nitrogen excretion in our cases agreed in general with the results of other observers, but as the quantity of nitrogen was not determined in the food of most of our cases, the total nitrogen values have no special significance. There was usually a rise in the excretion of total nitrogen during the third day, coincident with the greater uric acid excretion. But it was usually on this day that the secretion of the mother's milk began, and in consequence there was a greater nitrogen intake. After the third day the total nitrogen excretion was remarkably constant. In Case 9 (Protocol IX) the nitrogen balance was determined for three day periods.[39] The data are given in Table 9.

In Case 4 (Protocol IV) the nitrogen balance was determined for the first three days, with the following results:[40]

Milligrams of nitrogen ingested, 2,870; milligrams of nitrogen in urine and feces, 1,418; balance, +1,452=50.5 per cent. of the nitrogen ingested.

During the first three days there was a nitrogen retention in both infants in spite of the loss of weight during this period. Both infants, however, began to gain weight on the first day of the following period. The three infants observed by Langstein and Nieman[41] showed a nitrogen

39. The periods in this case were exactly 72 hours each. The food nitrogen was determined from a composite specimen of milk obtained by pumping the breasts before and after each nursing. There was very little colostrum in the breasts until the end of the second day. There were two feedings during the first day; subsequently the infant was nursed at three-hour intervals. The milk secretion began on the evening of the third day.

40. The period in this case was eighty-five hours. The determination of the food nitrogen and the technic of nursing was the same as in Case 9. There was a moderate amount of colostrum in the breasts. The milk secretion began about fifty-six hours post-partum, so that the infant's food during what is recorded as the third day (see Protocol IV), consisted, in part, of the first milk secretion.

41. Langstein and Nieman: Jahrb. f. Kinderh., 1910, lxxi, 604.

loss during the first three days. These infants, however, were not nursed by their own mothers but were fed on milk which had been pumped from wet-nurses.[42] Our patients ingested much more nitrogen during this period, since they received colostrum, which is much richer in nitrogen than mature milk.[43]

TABLE 9.—NITROGEN BALANCE IN CASE 9 DURING THE FIRST NINE DAYS OF LIFE

Period	Nitrogen Ingested Mg.	Nitrogen in Urine and Feces, Mg.	Balance Weight Mg.		Per cent. of Nitrogen Ingested
1	1,512	1,118	+394	=	26.
2	2,883	1,065	+1,818	=	63.
3	2,783	1,059	+1,724	=	61.9

During the second and third periods—from the fourth to the ninth days inclusive—there was a greater retention of nitrogen by Case 9 than by the cases of Langstein and Nieman. In one of their cases there was a nitrogen loss for the fourth and fifth days; in a second there was a negative balance for the sixth, seventh and eighth days. Michel[44] determined the nitrogen balance in one infant of four days, two of five days and one of seven days of age. The retention of the ingested nitrogen was 73 per cent., 75.7 per cent., 77.2 per cent., and 80 per cent., respectively. This higher nitrogen retention in Michel's cases was mainly due to the greater intake of nitrogen than in our case.

TABLE 10.—COMPARISON OF THE AVERAGE EXCRETION OF TOTAL NITROGEN TO TOTAL PURIN NITROGEN

	Immediate Ligation (4 Cases).			Late Ligation (5 Cases).		
Day	Total Nitrogen, Mg.	Purin Nitrogen, Mg.	Ratio P.N.:T.N., Mg.	Total Nitrogen, Mg.	Purin Nitrogen, Mg.	Ratio P.N.:T.N., Mg.
1.	197	25.4	1:7	172	24.7	1:7
2.	224	27.0	1:8	241	40.4	1:6
3.	249	33.9	1:7	332	43.9	1:7
4.	299	28.2	1:10	271	27.0	1:10
5.	294	22.2	1:13	327	18.5	1:17
6.	310	16.2	1:19	342	19.0	1:18
7.	344	15.2	1:22	274	16.1	1:17
8.	324	15.7	1:20	333	15.1	1:22

Phosphorus.—There have been only a few observations on the phosphorus excretion in the new-born, and these have given divergent results. Hecker[45] in an infant of 3 months, and Harley[46] in one of 6 months, found only traces of phosphorus. Martin and Ruge[5] and Parrot and

42. This insured a more accurate control of the quantity and composition of the food.

43. Langstein and Nieman point out the fact that their patients received a food poorer in nitrogen than they would if they had been nursed by their own mothers and had received colostrum, instead of a more mature milk.

44. Michel: Quoted by Keller, Arch. f. Kinderh., 1900, xxiv, 1; Czerny and Keller, 289 and 294.

45. Hecker: Virchow's Arch. f. path. Anat., 1857, xi, 217.

46. Harley: Quoted by Cruse (see note 29).

Robin[6] comment on the small phosphorus content of the urine of new-born infants. Cruse[29] states that phosphorus may be present only in traces in the urine of the new-born, or may be entirely absent. In his observations on the excretion of phosphates (uranium acetate titration) Cruse found from 0.008 to 0.039 per cent. in the urine of infants of 5 to 10 days of age, 0.010 to 0.058 per cent. in the urine of infants of 10 to 30 days, and 0.015 to 0.032 per cent. in the urine of infants 30 to 60 days of age. In one of the patients 5 days of age studied by Michel,[44] the average daily excretion of phosphorus was 22 mg. of P_2O_5 during a three-day period; a second infant 5 days of age excreted an average of 25 mg. of P_2O_5 a day during a four-day period. An infant of 7 days excreted a daily average of 34 mg. of P_2O_5 during a six-day period.

Moll[47] has recently emphasized the clinical importance of an estimation of the urinary phosphates. He states that the urine of a normal, thriving, breast-fed infant contains from 10 to 20 mg. of P_2O_5 a day, which type of urine he regards as being practically phosphorus-free, and 10 c.c. of which requires only a few drops of uranium acetate solution for the complete precipitation of the contained P_2O_5. It was observed that hunger had no effect on the phosphate elimination, but that there was a greatly increased elimination during "alimentary intoxication" (Finkelstein).

It was noted in our earlier cases in which the phosphorus was not determined (Protocols I, II, III and IV), that during the first few days the addition of the uranium acetate reagent of Folin and Shaffer produced a well-defined precipitate of uranium phosphate. During the later days the addition of this reagent produced, at most, a faint cloud and never a distinct precipitate. The total phosphorus was determined in four cases during three-day periods. The results are given in Table 11.

TABLE 11.—THE EXCRETION OF TOTAL PHOSPHORUS IN THE URINE OF CASES 6, 7, 8, AND 9, DURING THREE-DAY PERIODS

	P_2O_5 in Mg.				
Case	6	7	8	9	Average
Period 1. ...	46	44	63.4	60.7	53.5
Period 2. ...	Trace*	Trace*	Trace*	25.6	6.4
Period 3. ...	Trace*	4.2	11.8	27.2	10.8

*Gave a distinct precipitate of ammonium phospho-molybdate but the magnesium pyrophosphate precipitate was too small to weigh with accuracy. The phosphorus determinations were always made from as large a quantity of urine as possible; usually from one-fourth to one-half of the total urine for the period.

In Case 6 a daily determination was made after the third day. In Case 7 the phosphorus was determined in a composite specimen for the first three days, and for the seventh, eighth and ninth days, while a daily determination was made during the fourth, fifth and sixth days. In Cases 8 and 9 the phosphorus was determined in composite specimens for three-day periods. In Case 5 the urine of the second day was incomplete

47. Moll: Jahrb. f. Kinderh., 1909, lxix, 128.

and the phosphorus was determined in the composite specimen for the first and third, and the fourth and fifth days. The urinary phosphorus was as great during the fourth and fifth as during the first and third days. During the last day of observation the infant began to vomit and to suffer from a severe, watery diarrhea. This high phosphorus output on the fourth and fifth days is in marked contrast with the results in the other cases. This discrepancy may have been caused by an increased elimination of phosphorus, due to the gastro-intestinal disorder in harmony with Moll's view.

Langstein and Nieman[41] have determined the phosphorus elimination in three new-born infants, but their results differ considerably from ours. Their cases did not show a greater phosphorus elimination during the first three days, but on the contrary, the excretion usually increased after this time.

In Case 9 (Protocol IX) the phosphorus balance was determined. The results are given in Table 12.

TABLE 12.—THE PHOSPHORUS BALANCE IN CASE 9 DURING THREE-DAY PERIODS *

Period	P_2O_5 Ingested, Mg.	P_2O_5 in Urine and Feces, Mg.	Balance Weight, Mg.		Per cent. of P_2O_5 Ingested
1.	155.5	85.5	+ 70.	=	45.0
2.	492.9	67.9	+425.	=	86.2
3.	483.	88.8	+394.2	=	81.6

*The phosphorus content of the food was determined from a composite specimen of milk obtained by pumping the breasts before and after each nursing.

The percentage of phosphorus retained in this case closely corresponds with the results in Michel's[44] cases. Two infants of 5 days retained 87.3 and 77.3 per cent. of the phosphorus (P_2O_5) ingested; an infant of 7 days retained 80.1 per cent. of the phosphorus intake.

Acidity.—The acidity of the urine was determined in Case 8 by the method of Folin. Both the absolute and the percentage acidity were greatest during the first three days. The highest percentage acidity was on the second day, the greatest absolute acidity on the third day.

III. GENERAL CONSIDERATION OF THE URIC ACID EXCRETION AND THE CAUSATION OF THE URIC ACID INFARCTS

The results of Reusing, Sjöqvist and ourselves show that there is a comparatively abundant output of uric acid from the new-born. Those of Sjöqvist and ourselves show that this excretion is greatest during the period in which post-mortem examination and the occurrence of infarct elements in the urine indicate that uric acid is deposited in the kidney tubules. There are two possible explanations for the high uric acid output in the new-born: (1) a normal uric acid formation and a diminished destruction, or (2) increased formation with normal or diminished destruction.

Spiegelberg[48] found that when 0.1 gm. of uric acid per kilo of body weight was injected into young puppies, 53 per cent. was excreted in the urine, while in adult animals only 5.6 per cent. of the injected uric acid could be thus recovered. He was able to produce deposits of uric acid in the kidneys of puppies by the injection of quantities which were without effect on the older animals. He further observed that, after the uric acid injections, the urine of the puppies became cloudy, while that of the older animals remained clear. These experiments indicated that the young animals were less able to destroy uric acid than were the adults, and suggested that a deficient uric acid destruction was perhaps the explanation of the high excretion in the new-born. This explanation was supported by the studies of Mendel and Mitchell,[49] who observed that the uricolytic enzyme was the last to appear in the developing pig. Observations on the human organism, however, gave different results. Schittenhelm and Schmid[50] were able to show an active uricolysis by the organs of the fetus and the new-born infant. These results are of particular interest in contrast with the results of Schittenhelm,[51] and Künzel and Schittenhelm,[52] who were unable to demonstrate the presence of a uricolytic enzyme in the organs of adults. Wells and Corper[53] found no evidence of uricolytic activity in the organs of the fetus, the new born, or in those of adults. They therefore concluded that the human organism does not possess the ability to destroy uric acid. The results of Wiechowski[54] have a similar bearing, for he was able to recover in the urine a considerable portion of the uric acid injected into human beings (60 to 80 per cent.). Moreover, he was unable to demonstrate the presence of allantoin in the urine after the uric acid injections.

It seems, therefore, that the results of Spiegelberg on dogs are not applicable to the human organism. This variation is perhaps due to the fact that dogs normally have the power of destroying uric acid.

The second hypothesis—an increased uric acid formation—is favored by Reusing[15] and by Flensberg.[10] As shown by Gundobin,[37] Schiff[38] and others, soon after birth there is a rapid rise in the number of the leukocytes, which later shows a pronounced fall. The high uric acid formation was thus explained on the basis of Horbaczewski's theory.

The relationship of the leukocytes in the peripheral blood to the elimination of uric acid is a problem on which there is an enormous controversial literature, and which at the present time remains unsolved. There is little doubt that uric acid can arise from the nuclein of leukocytes, as

48. Spiegelberg: Arch. f. exper. Path. u. Pharmakol., 1898, xli, 428.
49. Mendel and Mitchell: Am. Jour. Physiol., 1907, xx, 97.
50. Schittenhelm and Schmid: Ztschr. f. exper. Path. u. Therap., 1907, iv, 424.
51. Schittenhelm: Ztschr. f. Physiol. Chem., 1909, lxiii, 248.
52. Künzel and Schittenhelm: Zentralbl. f. Physiol. u. Path. d. Stoffwech., 1908, iii, 721.
53. Wells and Corper: Jour. Biol. Chem., 1909, vi, 321.
54. Wiechowski: Arch. f. exper. Path. u. Pharmakol., 1909, lx, 185.

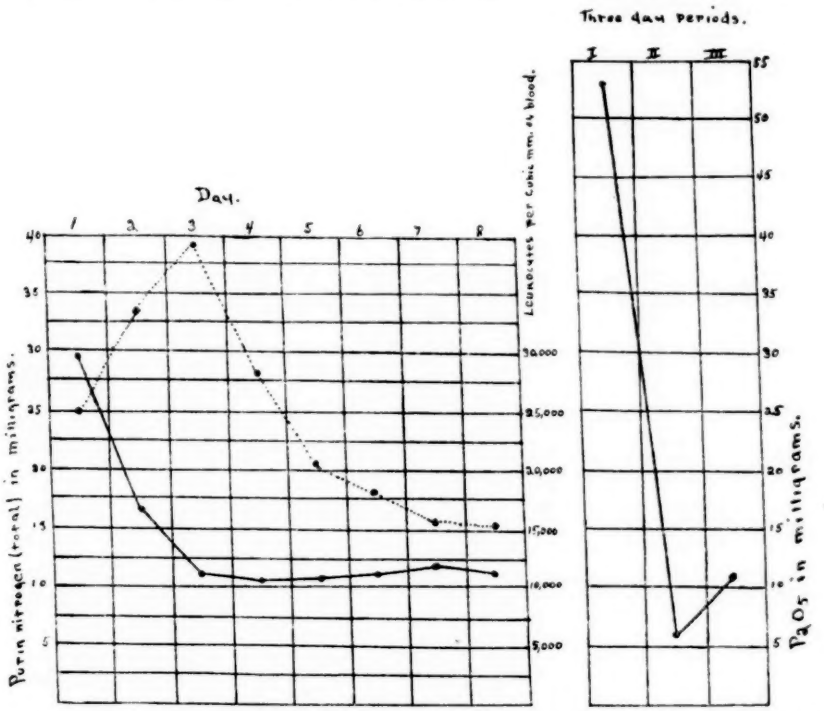
well as from the nuclein of other tissues. The observations of Fränkel,[55] Jakob,[56] Jakob and Krüger[57] and Musser and Edsall[58] in leukemia and of Kühnau[59] and others in pneumonia, gives evidence of the origin of uric acid from leukocytes. We have no evidence to show, however, that the number of leukocytes in the peripheral blood is an accurate index of the total number of these cells, nor that a decrease in the leukocyte count means a leukocyte destruction. It has been demonstrated by Goldscheider and Jacob,[60] Schulz,[61] Bohland[62] and others that a decreased number of leukocytes in the peripheral blood may only mean a changed distribution of these cells. These observers showed that when such a decrease was induced experimentally in animals, it was compensated by an accumulation of the leukocytes in the lung capillaries. In other words, these experiments indicate that fluctuations of the leukocyte count do not necessarily signify changes in the total number of these cells, but may merely indicate altered proportions in the peripheral circulation and the internal organs.

The apparent relationship of the leukocyte count to the uric acid excretion is shown by the tabulated data for our cases. There was usually an inverse ratio between the leukocyte count and the uric acid elimination during the first four days. There was a great decrease in the leukocyte value during the period when the uric acid figures were largest, which coincides with the time when the uric acid infarcts occur. The excretion of phosphorus followed a similar course; it was high during the first three days and then fell sharply to quantities which were often too small to estimate. It is well known that nuclear material is rich in phosphorus as well as in the precursors of uric acid, and this parallelism in the excretion of uric acid and phosphorus strongly suggests that their joint origin is from cell nuclei. It therefore seems correct to attribute the augmented uric acid excretion to an increased formation of that substance.

A more difficult problem arises when we attempt to determine whether this uric acid originates from leukocytolysis or finds its origin in other tissues. The high uric acid excretion occurs at a period when the blood is undergoing rapid morphologic changes. During fetal life and shortly after birth many of the red cells contain nuclei which disappear during the first few days of life. Shortly after birth the leukocytic formula shows a predominance of the polynuclear neutrophilic cells, but within

55. Fränkel: Deutsch. med. Wchnschr., 1895, xxi, 639.
56. Jakob: Arch. f. Physiol. u. Anat. (Dubois-Reymond), Physiol. Abth., 1894, 378.
57. Jakob and Krüger: Deutsch. med. Wchnschr., 1894, xx, 641.
58. Musser and Edsall: Univ. Penn. Med. Bull., 1905, xviii, 174.
59. Kühnau: Ztschr. f. klin. Med., 1897, xxxii, 482; Deutsch. Arch. f. klin. Med., 1897, lviii, 339.
60. Goldscheider and Jacob: Ztschr. f. klin. Med., 1894, xcviii, 373.
61. Schultz: Deutsch. Arch. f. klin. Med., 1893, li, 234.
62. Bohland: Centralbl. f. inn. Med., 1899, xx, 361.

a few days the proportion changes and the typical infantile blood picture —a predominance of lymphocytes—is apparent (Carstanjen[63]). There is at first an increase in the number of leukocytes in the peripheral blood, and later a pronounced decrease. It has been mentioned that when the new-born infant is left attached to the placenta some time after birth it receives a much larger amount of blood than when the umbilical cord is ligated immediately after birth. If the uric acid arises from the morphologic elements of the blood, it is to be expected that the excretion would be greater in the cases in which the umbilical cord was tied late.[64] That



Curve 1.—Comparison of the leukocytosis with the excretion of P_2O_5 and total purin nitrogen. Leukocytes, continuous line; total purin nitrogen, dotted line. The data for the purin nitrogen and leukocytes were obtained from all of the cases.

63. Carstanjen: Jahrb. f. Kinderh., 1900, liii, 215.

64. Reusing has suggested that the uric acid output should be greater in late ligation cases if the increased excretion of that substance in the new born originated from leukocytolysis; but he apparently made no observations bearing on this problem. The work of Hofmeier and Silvermann indicates that there is a destruction of the blood elements in icterus neonatorum. On the basis of this observation, Reusing has suggested that if the uric acid originates from a destruction of blood cells, there should be a greater excretion of uric acid by jaundiced infants. The two cases observed by Reusing give no conclusive evidence on this point. Two of our cases (Protocols IV and VII) developed a mild grade of icterus neonatorum. The degree of jaundice was very slight, however, and was evidenced only by a faint yellow color of the conjunctiva. In neither case was the excretion of uric acid greater than in the infants without jaundice.

this is the case is shown by the results from our cases. During the second and third days the average uric acid excretion, and the excretion in relation to the body weight, were greater in the late ligation cases. These observations would seem to indicate that the blood elements are in some way concerned with the increased uric acid formation in the new born. The pronounced decrease in the leukocyte count, and the disappearance of a great number of polynuclear cells from the peripheral blood, suggests that the uric acid arises from a leukocyte destruction. Although this evidence is suggestive, there is no proof that these changes signify a leukocyte destruction, and it is impossible to determine whether the uric acid arises wholly, or in part, from an increased number or an increased destruction of leukocytes, or from the extruded nuclei of the red cells. Perhaps it originates in some phase of metabolism concerned with the *production* of the formed elements of the blood.

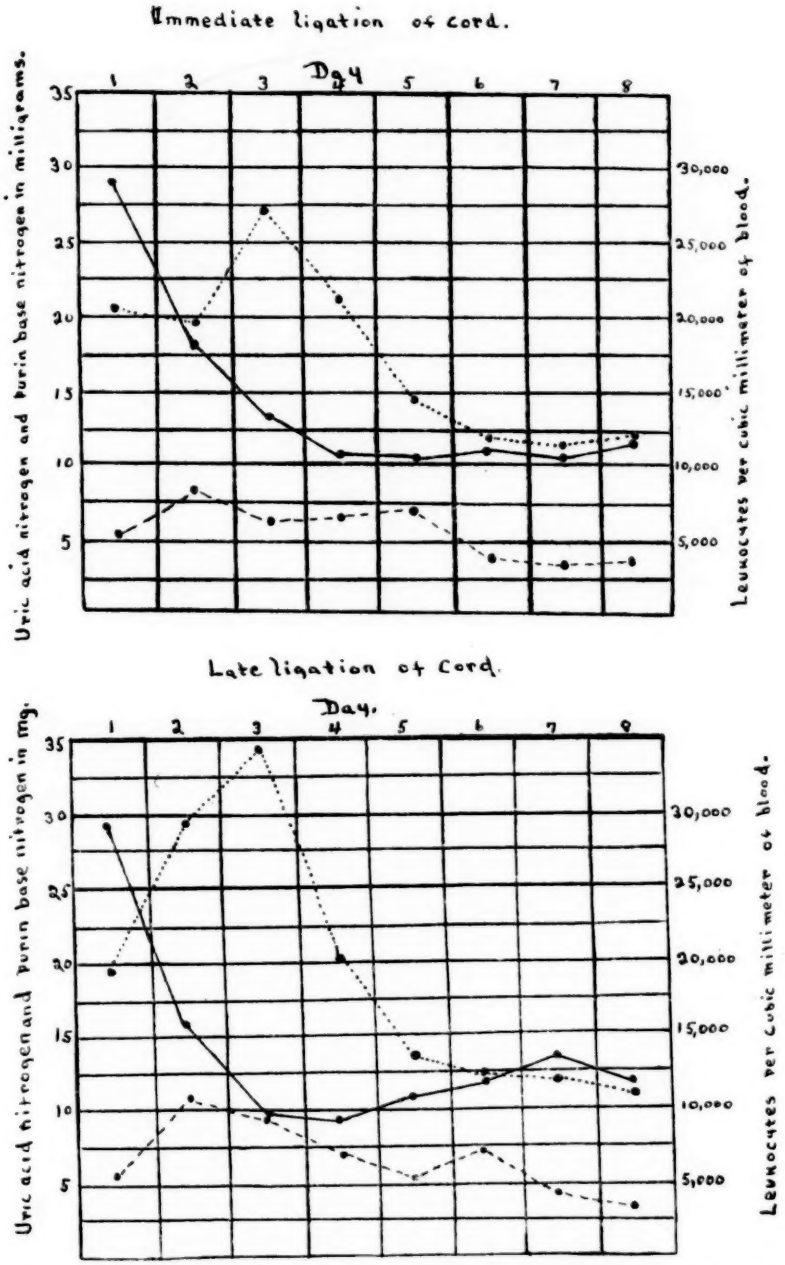
The exciting cause for the deposition of uric acid in the kidney tubules is not entirely clear. We found that the acidity of the urine was greatest during the first three days, which is coincident with the formation of the infarcts. This high acidity of the urine may be a factor in causing the deposition of uric acid, for uric acid is readily thrown out of solution by increased acidity of the urine.

Any acceptable hypothesis must explain not only the deposit of the uric acid in the kidney but also the formation of the infarct elements and stroma. The uric acid is not deposited directly in the kidney tubules but is found in the characteristic cylinders and spheres. There are certain objections to Ebstein's hypothesis—the primary deposit of uric acid and a secondary formation of the infarct stroma through cell necrosis. Spiegelberg has shown that the urine of the new-born infant has great solvent powers for uric acid, and that urine which was turbid with urates was still able to dissolve considerable quantities. It is also well known that the urine of adults may contain very large amounts of uric acid; yet uric acid infarcts never occur in adult life.

The explanation of Flensberg was based on careful histologic examination of the kidney of the fetus and the new-born infant. He showed the presence of the cylinders in the kidney tubules before the occurrence of the infarcts. It remains to be determined whether the contact of these cylinders with the concentrated and highly acid urine is sufficient to excite a deposit of uric acid on their surface, or whether the deposition of the uric acid depends on some special physical or chemical characteristic of the urine.

IV. SUMMARY AND CONCLUSIONS

1. Uric acid infarct elements were present in the urine of each of nine new-born infants.


Immediate ligation of cord.
Day.
1 2 3 4 5 6 7 8
35 30 25 20 15 10 5
Uric acid nitrogen and purin base nitrogen in milligrams.
30,000 25,000 20,000 15,000 10,000 5,000
Leukocytes per cubic millimeter of blood.
Late ligation of cord.
Day.
1 2 3 4 5 6 7 8
35 30 25 20 15 10 5
Uric acid nitrogen and purin base nitrogen in mg.
30,000 25,000 20,000 15,000 10,000 5,000
Leukocytes per cubic millimeter of blood.

Curve 2.—Relation of the number of leukocytes (continuous line) to the elimination of uric acid nitrogen (dotted line) and purin base nitrogen (broken line).

2. (a) The uric acid output in new-born infants is both absolutely and relatively high. It is greatest during the first three days and then decreases.

(b). In cases in which the umbilical cord was ligated late, the output of uric acid was greater during the second and third days than in cases in which the cord was ligated immediately after birth.

(c). The quantity of the purin substances in the colostrum ingested is too small to explain the observed high uric acid output.

3. The total phosphorus excretion was high during the first three days and then showed a sharp diminution. There is marked retention of phosphorus by the new-born infant.

4. There is a moderate nitrogen retention during the first three days of life. Later, nitrogen is retained in large degree.

5. There is an inverse ratio between the leukocyte count and the elimination of phosphorus and uric acid during the first few days of life.

6. In the light of our present knowledge, the parallelism between the excretion of uric acid and phosphorus during the first three days would seem to indicate a common origin from cell nuclei. The greater excretion of uric acid in the late ligation cases suggests that the formed elements of the blood in some way serve as its origin.[65]

We desire to thank Professor Gies for his kindness in placing the facilities of his laboratories at our disposal, and to acknowledge our great indebtedness to him and his associate, Dr. J. Rosenbloom, for much valuable assistance. We wish also to acknowledge our indebtedness to Dr. Rowland G. Freeman for permitting us to use the material from his service at the New York Nursery and Child's Hospital, and to thank the superintendent and nurses for their cooperation. We are also greatly indebted to Mr. F. W. Shaffer for much assistance in the supervision of the cases from the Nursery and Child's Hospital, and to Miss R. Feagin for her careful supervision of Case 9.

54 West One Hundred and Fourth Street—Troy, Texas.

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65. In addition to the numbered references the following have been freely consulted:

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PROTOCOL I.—CASE 1.—IMMEDIATE LIGATION OF UMBILICAL CORD, FIRST CHILD

Day	Weight, Gm.	Urine: Specific Gravity	Urine: Quantity c.c.	Urine: Uric Acid Mg.	Urine: Purin* Base Nitrogen, Mg.	Urine: Total Nitrogen, Mg.	Leukocytes per c.mm. of Blood
1. 38 hours	3,642	1014	32	43.	2.3	136.	28,100
2.	3,494	1018	25	23.8	2.3	148.2	14,000
3.	3,494	1011	130	101.6	4.7	269.4	17,400
4.	3,614	1004	280	98.5	12.9	243.1	14,200
5.	3,676	1005	350	75.2	12.9	199.6	12.700
6.	3,616	1005	290	45.3	4.5	284.1	8,000
7.	3,676	1004	290	43.8	6.5	310.	11,700
8.	3,676	1004	360	50.6	4.9	308.1	11,000

*Daily determination by Kenneway's modification of the Cammerer-Arnstein method.

PROTOCOL II.—CASE 2.—LATE LIGATION OF UMBILICAL CORD. SECOND CHILD

Day	Weight, Gm.	Urine: Specific Gravity	Urine: Quantity c.c.	Urine: Uric Acid Mg.	Urine: Purin* Base Nitrogen, Mg.	Urine: Total Nitrogen, Mg.	Leukocytes per c.mm. of Blood
1. 25 hours	3,568	1016	30	47.5	3.7	127.6	24,500
2.	3,269	1010	32	76.5	2.7	142.	14,300
3.	3,227	1010	part lost	....	....	.....	7,300
4.	3,269	1007	310	77.5	7.1	220.	7,600
5.	3,227	1005	310	53.7	1.4	310.8	7,500
6.	3,255	1005	part lost	....	....	.....	12,600
7.	3,295	1005	268	50.	4.3	196.4	13,200
8.	....	....	...	.....	....	.....	11,400

*Daily determination by Kenneway's modification of the Cammerer-Arnstein method.

PROTOCOL III.—CASE 3.—LATE LIGATION OF UMBILICAL CORD. FIRST CHILD

Day	Weight, Gm.	Urine: Specific Gravity	Urine: Quantity c.c.	Urine: Uric Acid Mg.	Urine: Total* Purin Nitrogen, Mg	Urine: Total Nitrogen, Mg	Leukocytes per c.mm. of Blood
1. 24 hours	3,479	1020	12	37.8	....	169.4	38,000
2.	3,367	1012	110	142.5	73.8	342.1	15.800
3.	3,367	1007	210	104.16	49.7	326.2	11,600
4.	3,339	1005	280	56.6	22.6	266.5	11,000
5.	3,425	1005	370	37.	14.3	355.8	14,000
6.	3,425	1007	365	42.8	18.5	347.4	14,400
7.	3,507	1005	275	31.	14.1	261.8	17,900
8.	3,624	1004	390	29.9	12.2	371.2	13,700

*Daily determination by the method of Krüger and Schmid.

PROTOCOL IV.—CASE 4.—IMMEDIATE LIGATION OF UMBILICAL CORD. SECOND CHILD. VERY SLIGHT DEGREE OF ICTERUS NEONATORUM

Day	Weight, Gm.	Food			Urine					Feces			Leukocytes per c.mm. of Blood
		Quantity, Gm.	Purin Nitrogen, Mg.	Total Nitrogen, Mg.	Specific Gravity	Quantity c.c.	Uric Acid, Mg.	Total* Purin Nitrogen, Mg.	Total Nitrogen, Mg.	Total Nitrogen, Mg.	Purin Nitrogen, Mg.	Nitrogen Balance Mg.	
1. 37 hours	4,200	135.	....	.....	1012	72	62.7	23.2	295.4	.....	....	.....	21,000 32,000
2.	4,050	291.5	....	.....	1020	43	86.3	39.1	294.1	.....	....	.....	14,800
3.	3,900	310.	....	.....	1009	112	72.	27.7	286.	.....	....	.....	12,100
For period	...	.....	27.6	2,870	....	...	....	....	.....	543.7	11.6	+1.452	.....
4.	3,930	.....	....	.....	1006	249	50.5	19.1	355.4	.....	....	.....	8,700
5.	3,990	.....	....	.....	1005	415	30.4	13.8	340.6	.....	....	.....	9,800
6.	4,020	.....	....	.....	1005	450	36.0	14.0	348.3	.....	....	.....	11,000
For period	...	.....	....	.....	....	...	....	....	.....	587.6	4.2	.....	.....
7.	4,140	.....	....	.....	1005	410	41.	15.4	348.3	.....	....	.....	7,500
8.	4,230	.....	....	.....	1005	400	31.2	14.8	361.6	.....	....	.....	8,000
For period	...	.....	....	.....	....	...	....	....	....	141.3	6.4	.....	.....

*Daily determination by the method of Krüger and Schmid.

PROTOCOL V.—CASE 5.—IMMEDIATE LIGATION OF UMBILICAL CORD. FIRST CHILD

Day	Weight, Gm.	Food: Quantity, Gm.	Food: Purin Nitrogen Mg.	Urine: Specific Gravity	Urine: Quantity c.c.	Urine: Uric Acid, Mg.	Urine: Purin* Base Nitrogen, Mg.	Urine: Total Nitrogen, Mg.	Urine: P_2O_5, Mg.	Feces: Total Nitrogen, Mg.	Feces: Purin Nitrogen, Mg.	Leukocytes per c.mm. of Blood
1. 25 hours	3,201	...	....	1011	28.5	28.5	....	173.8	....	.....	....	16,500** 26,500† 29,800‡
2.	3,100	120	....	1014	part lost	....	....	.....	....	.....	....	21,200
3.	3,060	280	....	1011	75.	76.2	....	221.1	....	.....	....	15,575
For period	...	...	13.4	....	....	....	18.1	.....	37.4	306.1	12.2	.....
4.	3,120	...	....	1010	92.	61.	....	312.8	....	.....	....	7,200
5.	3,150	...	....	1008	170.	40.4	....	297.2	....	.....	....	8,700
For period	...	...	....	....	....	....specimen lost.....			36.9	192.	4.9	.....

*Determined in the composite specimen by Kenneway's modification of the Cammerer-Arnstein method.

**Half hour after birth. †Seven hours after birth. ‡Fourteen hours after birth.

PROTOCOL VI.—CASE 6.—LATE LIGATION OF UMBILICAL CORD. FIRST CHILD

Day	Weight, Gm.	Food: Quantity, Gm.	Food: Purin Nitrogen, Mg.	Urine: Specific Gravity	Urine: Quantity, c.c.	Urine: Uric Acid, Mg.	Urine: Purin Base* Nitrogen, Mg.	Urine: Total Nitrogen, Mg.	Urine: P_2O_5, Mg.	Feces: Total Nitrogen, Mg.	Feces: Purin Nitrogen, Mg.	Leukocytes per c.mm. of Blood
1. 22 hours	3,900	20	....	1020	19	29.2	....	134.4	..	.....	....	17,175‡ 32,345§ 25,100¶
2.	3,600	190	....	1015	70	68.7	....	286.8	..	.....	....	19,100
3.	3,570	300	....	1009	130	105.3	....	360.5	..	.....	....	11,500
For period		...	18.3	....	...	.....	9.3	.....	46	918.3	15.3	.....
4.	3,690	...	....	10045	335	71.9	....	385.4	Trace†	.....	....	10,600
5.	3,780	...	....	1004	300	30.	....	340.	Trace†	.....	....	11,500
6.	3,870	...	....	1005	360	30.2	....	297.8	Trace†	.....	....	11,000
For period		...	....	.....	...	.....	37.4	.....	..	.....	....	.....
7.	3,840	...	....	1006	400	32.6	....	367.6	Trace†	.....	....	11,800
8.	3,885	...	....	1006	380	36.1	....	310.2	Trace†	.....	....	11,400
For period		...	....	.....	...	.....	14.	.....	..	.....	....	.....

*Determined in the composite specimen by Kenneway's modification of the Cammerer-Arnstein method.

†Molybdate precipitate very light; no weighable $Mg_2P_2O_7$.

‡Two hours after birth. §Seven hours after birth. ¶Fourteen hours after birth.

PROTOCOL VII.—CASE 7.—IMMEDIATE LIGATION OF UMBILICAL CORD. FIRST CHILD. VERY SLIGHT DEGREE OF ICTERUS NEONATORUM

		Food		Urine						Feces		
Day	Weight, Gm.	Quantity, Gm.	Purin Nitrogen, Mg.	Specific Gravity	Quantity, c.c.	Uric Acid, Mg.	Purin* Base Nitrogen, Mg.	Total Nitrogen, Mg.	P_2O_5, Mg.	Total Nitrogen, Mg.	Purin Nitrogen, Mg.	Leukocytes per c.mm. of Blood
1. 38 hours	3,479	80	....	1016	47	108.9	....	179.	..	.....	....	19,900‡ 24,500§ 23,900¶
2.	3,367	190	....	1018	75	62.6	....	230.1	..	.....	....	21,800
3.	3,227	230	....	1010	114	79.5	....	220.6	..	.....	....	10,200
For period	...	...	23.1	....	...	.....	33.4	.....	44	814.8	18.3	.....
4.	3,255	240	....	1008	190	46.2	....	286.2	Trace†	.....	....	13,100
5.	3,255	...	....	1008	230	33.8	....	343.1	Trace†	.....	....	9,900
6.	3,339	...	....	1007	300	29.2	....	298.4	Trace†	.....	....	14,300
For period	...	...	....	....	...	.....	16.7	.....	..	.....	....	.....
7.	3,395	...	....	1007	375	23.	....	386.4	..	.....	....	11,600
8.	3,395	...	....	1006	340	28.5	....	310.4	..	.....	....	15,000
9.	3,451	...	....	1006	375	29.2	....	301.2	..	.....	....	17,000
For period	...	...	....	....	...	.....	4.1	.....	4.2§§	....	....	.....

*Determined in the composite specimen by Kenneway's modification of the Cammerer-Arnstein method.
†Slight molybdate precipitate; no weighable $Mg_2P_2O_7$. ‡One hour 40 minutes after birth.
§Eighteen hours after birth. §§425 c.c. of urine used for determination. ¶Twenty-four hours after birth.

PROTOCOL VIII.—CASE 8.—LATE LIGATION OF UMBILICAL CORD. FIRST CHILD

Day	Weight Gm.	Urine: Specific Gravity	Urine: Quantity, c.c.	Urine: Uric Acid, Mg.	Urine: Purin* Base, Nitrogen, Mg	Urine: Total Nitrogen, Mg.	Urine: P_2O_5† Mg.	Acidity§: Per 100	Acidity§: Total	Leukocytes per c.mm. of Blood
1. 31 hrs.	3,110	1012	43	116.9	....	158.4	....	27.40	11.78	22,800
2.	3,110	1015	39	68.4	....	198.9	....	41.76	16.28	13,600
3.	2,998	10075	240	98.4	....	312.7	....	7.76	18.61	9,300
For period.	...	....	...	.....	33.8	.....	63.4	.....	.....	.....
4.	2,970	1008	182	36.2	....	216.5	....	5.24	9.53	10,000
5.	2,879	1007	222	40.6	....	314.5	....	4.96	11.01	11,600
6.	2,942	1007	270	35.9	....	382.5	....	5.24	14.14	11,500
For period	...	....	...	.....	14.8	.....	Trace‡	.....	.....	.....
7.	2,998	1007	275	31.6	....	374.	....	4.96	13.64	12,700
8.	3,044	1007	290	40.	....	328.8	....	4.96	14.38	11,600
9.	3,044	1007	320	29.4	....	253.7	....	3.54	11.32	9,700
For period	...	....	...	.....	3.4	.....	11.8	.....	.....	.....

‡Slight molybdate precipitate; No weighable $Mg_2P_2O_7$.

§In cubic centimeters of N/10 NaOH.

*Determined in the composite specimen by Kenneway's modification of the Cammerer-Arnstein method.

†The urine used for the determination of the acidity was afterwards used in the phosphorus determination. Since free oxalic acid interferes with the precipitation of ammonium phosphomolybdate, blank determinations were made. Duplicate phosphorus determinations were made in a solution of sodium dihydrogen phosphate with the following results:

	Magnesium Pyrophosphate, Gm.
1. 25 c.c. of phosphate solution	0.0395
	0.0398
2. 25 c.c. of phosphate solution with the addition of nitric and sulphuric acids	0.0396
Not heated	0.0389
3. 25 c.c. of phosphate solution with the addition of nitric and sulphuric acids and 10 gm. of potassium oxalate	*No molybdate precipitate.*
Not heated.	
4. 25 c.c. of phosphate solution with the addition of nitric and sulphuric acids and 10 gm. of potassium oxalate	0.0397
Heated as in the Neuman oxidation method	0.0391

It is thus seen that when the Neuman method of oxidation is used, the presence of oxalic acid does not interfere with the determination.

PROTOCOL IX.—Case 9.—Late Ligation of Umbilical Cord. First Child

Day	Weight Gm.	Food				Urine						Feces					Nitrogen Balance Mg.	Phosphorus Balance Mg.	Leukocytes per c.mm. of Blood
		Quantity, Gm.	Total Nitrogen, Mg.	Purin Nitrogen, Mg.	P_2O_5, Mg.	Quantity, c.c.	Specific Gravity	Total Nitrogen, Mg.	Purin Nitrogen * Absolute, Mg.	Purin Nitrogen * As Uric Acid, Mg.	P_2O_5, Mg.	Total Nitrogen, Mg.	P_2O_5, Mg.						
1. 24 hours	3,600	15	....	....	....	32	1013	168.3	23.8	71.4	....	....	....				.....	....	39,000
2.	3,500	100	....	....	....	40	1017	146.2	29.2	87.6	....	....	....				.....	....	26,000
3.	3,230	140	....	....	....	120	1017	284.	41.9	125.7	....	....	....				.....	....	14,000
For period	...	...	1,512	11.9	155.5	...	....	....	....	....	60.7	520.	24.8		+ 394	+ 70	.....		
4.	3,260	290	....	....	....	200	1008	310,3	26.	78.0	....	....	....				.....	....	14,300
5.	3,260	310	....	....	....	220	1008	297.4	21.3	63.9	....	....	....				.....	....	10,100
6.	3,300	330	....	....	....	260	1006	318.6	16.6	49.8	....	....	....				.....	....	8,000
For period	...	...	2,883	16.7	492.9	...	....	....	....	....	25.6	141.1	42.3		+1,818	+425	.....		
7.	3,390	360	....	....	....	280	1005	299.8	16.1	48.3	....	....	....				.....	....	10,400
8.	3,430	360	....	....	....	240	1004	308.5	14.9	44.7	....	....	....				.....	....	12,200
9.	3,520	430	....	....	....	300	1004	313.4	16.0	48.0	....	....	....				.....	....	9,800
For period	...	...	2,783	8.08	483.	...	....	....	....	....	27.2	139.6	61.6		+1,724	+395	.....		

*Daily determination by the method of Krüger and Schmid.

THE NON-SPECIFICITY OF THE CYTO-FINDINGS IN THE SPINAL FLUID IN VARIOUS MENINGEAL CONDITIONS, ESPECIALLY IN CHILDREN

FROM AN EXAMINATION OF OVER FIVE HUNDRED SPECIMENS

WILLIAM PALMER LUCAS, M.D.
BOSTON

Text-books which deal with the examination of the spinal fluid give much space to elaborate schemes for a positive diagnosis from the spinal fluids in the different forms of meningitis. However, if one has had these same spinal fluids to examine, one is immediately impressed with the fact that no absolute rules will hold. This is especially true in cases of suspected tuberculous meningitis. Several recent articles have claimed a cure in cases of tuberculous meningitis, the diagnosis of which has been based on the mere counting of the cells, and a differential study of these cells.

In direct opposition to this point of view it may be interesting to note the findings in several different conditions, that have come under observation, which commonly occur in children.

The diagnosis of epidemic meningococcus meningitis is never based solely on the finding of an excess of polynuclears in the exudate. The infecting organism is the most important finding, and on it is based not only the treatment, but also the prognosis.

Nor is one justified in diagnosing a case as one of tuberculous meningitis because the fluid contains a preponderance of mononuclear cells, or lymphocytes. The etiologic causes underlying these findings are, to be sure, very much harder to determine than in the instance of fluids in which the organism is easily discoverable, and almost as easily identified. But even in long continued pyogenic infections in which the process has become chronic, the reversion from a polynuclear to a mononuclear predominance is seen. Just why this reaction should occur may not be perfectly clear, but still it remains a fact that in this respect the reaction of the meninges resembles that of the true serous membranes, pleural, pericardial and peritoneal, and even the synovial membranes.

All these membranes react in a more or less parallel and uniform way to various infecting agents. Each membrane is, of course, governed by certain definite, normal conditions. Understanding and realizing these normal limits and conditions is essential in understanding the reactions to certain infectious agents. The reason why certain infectious

agents act as they do on these different membranes is not nearly so clear. The exact reasons for these chemotactic properties depend, undoubtedly, on certain factors in protective immunity, of which as yet little is known. It is true of all this group of membranes that the pyogenic organisms at first exert a polynuclear chemotaxis, and if they become chronic, a mononuclear chemotaxis replaces the original polynuclear one.

It is equally true that certain other organisms (*Spirochæta pallida*, tubercle bacillus) and certain toxins and viruses (toxins of almost any pyogenic organism, e. g., pneumococcus, see Cases 1, 7 and 8, Table 3; the virus of rabies and epidemic myelo-encephalitis [anterior poliomyelitis]) produce a mononuclear, or lymphocytic chemotaxis. It is quite as erroneous to pronounce a diagnosis of tuberculous meningitis from the cytologic picture of a mononuclear predominance in the fluid, as it would be to pronounce a case meningococcus meningitis from the polynuclear excess. True, in both cases, due to the predominance of these two types of infection, one might be right in his diagnosis, and still be working in the realm of guess-work.

In an earlier article[1] attention was called to the occurrence of encephalitis in children, and also to the fact that the findings in the spinal fluid in such cases were identical in many cases with those found in tuberculous meningitis. The spinal fluid in such cases was identical in many cases with that found in tuberculous meningitis. The spinal fluid in encephalitis is increased in amount and is under pressure, and may be opalescent, or even slightly turbid from the excess of cells found in the fluid, which are mainly of the mononuclear and lymphocytic type.

Table 1, showing cases of encephalitis, from the Children's Hospital, occurring during the past four years, will perhaps make these points more clear. To this class probably belong the majority of cases of mistaken diagnosis.

The recent studies in epidemic myelo-encephalitis (anterior poliomyelitis) by Flexner and Lewis, in this country, have brought this epidemic disease very prominently before the medical profession. In an attempt to get some points in the early diagnosis of this condition I have been able to show both by experimental means,[2] in spinal fluids from monkeys, and from the spinal fluid in eleven cases of undoubted, and several cases of abortive, myelo-encephalitis in children, the occurrence in the spinal fluid of large numbers of mononuclear cells, or

1. Southard, E. E., and Lucas, William P.: Encephalitis in Children, with Reference to Frequency of Epilepsy following Recovery. (Unpublished.)

2. Lucas, W. P.: The Diagnosis of Infantile Paralysis in the Prodromal and Early Acute Stage as Found in the Experimental Study of Acute Poliomyelitis in Monkeys, with Reports of Findings in Four Human Cases. *Boston Med and Surg. Jour.*, 1910, clxiii, 245; Gay, Frederick P., and Lucas, William P.: Anterior Poliomyelitis, Methods of Diagnosis from Spinal Fluid and Blood in Monkeys and Human Beings, *Arch Int. Med.*, 1910, vi, 330.

TABLE 1.—Age, Onset, Physical Signs and Findings in the Cerebrospinal Fluid in Twelve Cases of Encephalitis

Case No.	Age	Onset	Nervous Symptoms	Reflexes	Amount c.c	Pressure	Character	Clot Formation	Cell Count per c.mm.	Differential
1	2 yrs.	Sudden.	Convulsions.	Kernig on left side; rigidity of neck.	30	Moderate.	Slightly opalescent.	Fine clot.	400	Mononuclears in excess.
2	6½ yrs.	Gradual.	Stupor.	Ptosis of right eyelid.	40	Moderate.	Clear.	Fine clot; fibrin shreds.	50	Lymphocytes.
3	4 yrs.	Gradual.	Convulsions.	Kernig sign present; aphasia.	20	Slight.	Clear.	Fine clot.	80	Mononuclears 80 %.
4	3 yrs.	Gradual.	Stupor.	Rigidity of neck.	10th day, 30 19th day, 25	Moderate. Moderate.	Opalescent. Opalescent.	Moderate. Slight.	120 160	Polynuclears 55 %. Mononuclears 45 %.
5	2½ yrs.	Sudden.	Dull.	Neck sign present.	35	Moderate.	Clear.	None.	10	All mononuclears.
6	4 yrs.	Sudden.	Dull.	Neck rigid; neck sign present.	45	Marked.	Clear.	Spider-web clot.	20	Polys. and monos. equal.
7	2 yrs.	Sudden.	Delirious.	Photophobia; neck sign and Kernig present.	30	Moderate.	Opalescent.	Spider web.	480	Mononuclears 97 %.
8	4 yrs.	Sudden.	Convulsions.	Strabismus; choked disk.	25	Moderate.	Opalescent.	Slight.	185	Mononuclears 85 %.
9	3 yrs.	Sudden.	Convulsions.	Rigidity of neck; facial paralysis; strabismus.	40	Marked.	Slightly opalescent.	Moderate.	82	Mononuclears 95 %.
10	5 yrs.	Sudden.	Marked pain.	Rigidity of neck; strabismus.	25	Moderate.	Opalescent.	Moderate.	200	Lymphocytes 100 %.
11	4 yrs.	Slow.	Sensitive.	Absent.	50	Marked.	Clear.	None.	25	Lymphocytes 95 %.
12	1 yr.	Sudden.	Convulsions.	Absent; pupils unequal and sluggish.	10	Normal.	Clear	Small clot.	40	All mononuclear.

TABLE 2.—Findings in Eleven Cases of Epidemic Myelo-Encephalitis[3]

Case No.	Age	Onset	Nervous Symptoms	Reflexes	c.c. Amt.	Pressure	Character	Spinal Fluid Clot Formation	Cells per cu.mm.	Differential Cell Count	Result
1	3 yrs.	Gradual.	Irritable.	Absent k. j's; very sensitive.	20	Slight.	Clear.	None.	180	Mononuclear 100 %.	Recovered.
2	9 mos.	Gradual.	Irritable.	Absent; very sensitive.	35	Marked.	Opalescent.	Present; fine clot.	580	Mononuclear 97 %.	Recovered.
3	5 yrs.	Gradual.	Irritable.	Absent; very sensitive.	50	Marked.	Opalescent.	Small clot; fibrin shreds.	510	Mononuclear 93 %.	Recovered.
4	2 yrs.	Sudden.	Irritable.	Absent; sensitive.	30	Moderate.	Clear.	Spider-web clot.	130	Mononuclear 87 %.	Recovered.
5	5 yrs.	Sudden.	Irritable.	Very sensitive.	40	Marked.	Slightly opalescent.	Fine clot.	250	Mononuclear 89 %.	Recovered.
6	4 yrs.	Sudden; convulsions.	Irritable; convulsions.	Kernig present; neck sign present; neck rigid.	30	Moderate.	Clear.	No clot, but fibrin shreds.	90	Mononuclear 100 %.	Recovered.
7	4 yrs.	Sudden.	Irritable.	Absent.	45	Marked.	Slightly opalescent.	Spider web clot.	120	Mononuclear 95 %.	Recovered.
8	7 yrs.	Fairly rapid.	Irritable; coarse tremors.	Absent; sensitive.	50	Marked.	Opalescent.	Spider-web clot and fibrin shreds.	210	Mononuclear 97 %.	Recovered.
9	3 yrs.	Sudden.	Irritable.	Absent; sensitive.	30	Slight.	Slightly turbid.	Moderate clot.	70	Mononuclear in exces	Recovered.
10	9 yrs.	Sudden.	Irritable; sensitive.	Double Kernig; neck sign.	40	Moderate.	Clear.	Fibrin shreds.	200	Mononuclear 75 %.	Died.
11	3 yrs.	Sudden.	Irritable.	Double Kernig; sensitive.	35	Slight.	Opalescent.	Spider web.	55	Mononuclear 87 %.	Died.

3. Most of these spinal fluids were sent me for examination by the Massachusetts State Board of Health, to which I am indebted for the privilege of having had this opportunity of studying the spinal fluid from early human cases.

TABLE 3.—Meningism or Toxic-Meningeal Irritation During Infectious Diseases

Case No.	Age	Onset	Mental Condition	Reflexes	Amount, c.c.	Pressure	Character	Clot Formation	Cell Count per cu.mm.	Differential
1	2 yrs.	Pneumonia.	Stupor.	Rigidity of neck; Kernig sign.	First exam., 20 Second exam., 40	None. Moderate.	Clear. Opalescent.	None. Spider web.	5 40	All lymphocytes. All lymphocytes.
2	2¾ yrs.	Infectious diarrhea.	Dull; delirious; convulsions.	Neck sign; Kernig sign.	15	Slight.	Clear.	Fibrin shreds.	45	All mononuclear.
3	5 mos.	Pertussis.	Delirious.	Kernig; rigidity of neck.	6	None.	Clear.	Small clot.	10	All lymphocytes.
4	20 mos.	Otitis media.	Dull; delirious.	Muscular tremors; rigidity of neck.	10	Slight.	Clear.	Fibrin shreds.	90	All lymphocytes.
5	3 mos.	Otitis media.	Delirious; convulsions.	Muscular twitchings; Kernig; neck sign.	First exam., 30 Third exam., 14	Marked. Slight.	Clear. Clear.	Fibrin shreds. Fibrin shreds.	80 20	Lymphocytes 90 %. All lymphocytes.
6	4 yrs.	Secondary anemia.	Dull; semiconscious.	Flaccid; all absent.	10	Slight.	Opalescent.	Small clot.	200	Polynuclears 61 %. Mononuclears 39 %.
7	5 yrs.	Lobar pneumonia.	Convulsion.	Kernig; neck sign; rigidity of neck.	20	None.	Clear.	None.	50	Lymphocytes in excess.
8	6 yrs.	Lobar pneumonia.	Delirious; convulsions.	Rigidity of neck; Kernig.	80	Moderate.	Opalescent.	Fibrin shreds.	80	Lymphocytes in excess.

lymphocytes, the occurrence also of fibrin, and a turbidity as marked as is found in any case of tuberculous meningitis.

Table 2 will show these findings and the different degrees of variation which each may undergo.

A third series of cases is reported (Table 3) which do not occur as often as the first two series, especially at the time of an epidemic. However, it is a condition that occurs frequently in acute infections, and which commonly gives a spinal fluid identical with that found in tuberculous meningitis, except for the absence of the tubercle bacillus.

It is plain from the study of these three tables that the spinal fluid reacts in the same way to a group of very different infections. Similar tables could be made from still more widely differing conditions as, for instance, syphilis. But as cerebral syphilis, or syphilis of the central nervous system, is rare in children, I have had the opportunity of examining only one such fluid, in which there was an increase in the mononuclear cells as well as an increase in the amount and pressure, but without any clot formation.

A study of 248 cases of tuberculous meningitis, with over 300 spinal fluid examinations shows the wide range of difference in the special observations and brings out the following points of interest:

The amount varied from 5 c.c. to 120 c.c., with occasionally dry taps. The fluid was usually clear to opalescent, but on several occasions turbid fluid was reported with very high cell-counts. Clot formation was absent in a little less than 10 per cent. of the examinations, but was usually present at some one of the examinations in every case. The clot also varied from the typical spider-web clot which forms in the course of several hours to one that forms almost immediately, and is of a pronounced gelatinous character. The cell count, which is made in one of the ordinary counting chambers, varied from fourteen to 920 cells per cu. mm., the average being 206 cells per cu. mm.; but 50 per cent. of the counts were 100, or below, so that such a high average is very misleading.

The differential count varied between 100 per cent. of lymphocytes and mononuclears and 89 per cent. of polynuclears, to 11 per cent. of mononuclears in one case. There were twenty-five instances in which the percentage of polynuclears was 30 per cent. or over. On repeated examinations this, however, would revert to the ordinary mononuclear count of over 90 per cent.

In a study of 102 cases from different forms of pyogenic meningitis, the epidemic meningococcus meningitis predominated; the findings also varied over a fairly wide range. The amounts varied from simply a slight amount of exudate in the needle to 250 c.c. of turbid fluid. In three cases only has clear fluid been found with the

TABLE 4.—FINDINGS IN THE SPINAL FLUID IN THE VARIOUS TYPES OF MENINGITIS

Types	Amount of Spinal Fluid c.c.	Pressure	Character of Fluid	Presence of Fibrin	Cell Count per c.mm.	Differential Count	Organisms
Tuberculous meningitis.	10 to 100	Moderate.	Clear to opalescent.	On standing, fine clot.	15 to 200	Mononuclears predominating except in few acute cases.	Tubercle bacillus.
Epidemic cerebrospinal meningitis.	10 to 100	Marked.	Cloudy.	Marked.	100 to 800	Polynuclears predominating except in chronic stage.	*Diplococcus intracellularis.*
Pneumococcus and streptococcus.	+ to 100	Marked.	Cloudy.	Marked.	100 to 800	Polynuclears predominating.	Pneumococcus, streptococcus.
Other meningitis.	+ to 100	Marked.	Opalescent. to cloudy.	Marked.	40 to 400	Polynuclears predominating; in influenza at times mononuclears predominating.	Various organisms.
Encephalitis.	10 to 80	Slight.	Clear.	Absent to slight.	10 to 100	Mononuclears.	None.
Anterior poliomyelitis.	10 to 50	Slight.	Clear.	Present early; absent late.	10 to 100	Mononuclears during acute stage; polynuclears late if at all.	None.
Meningismus or toxic meningeal irritation.	Slightly plus.	Slight.	Clear.	Uusually absent; occasionally very small clot or shreds of fibrin.	10 to 80	Mononuclears.	None.
Normal.	5 to 10	None.	Clear.	Absent.	1 to 5 per cu. mm.	Mononuclears or endothelial cells.	None.

presence of the meningococcus. The clot formation was always present in abundance in all except these three cases, in which the clot was very fine, and resembled in every way that of the other types of meningeal irritation mentioned. The cell-count varied from forty-five cells per cu. mm. to 2,600, and in many cases the exudate was too thick to make even an approximate count. The differential count almost invariably gave a preponderance of polynuclear cells. In the chronic ones the mononuclear cells usually were equal to or in excess of the polynuclear cells; and during the treatment of meningococcus meningitis by its specific antiserum, the mononuclears would increase to the same extent as in the chronic cases.

Table 4 shows the wide range of findings in the spinal fluid from the cases discussed and shows very clearly the non-specific character of the cell-findings. It is evident from this study that the study of cell morphology alone in the spinal fluid of different meningeal conditions is not sufficient to separate the different types of meningitis, and therefore the diagnosis can never be based on this. The infecting or causative organism must be found in all cases in which there is a direct infection. A negative finding gives very little aid toward the positive diagnosis, though it has a value which increases with the clinical study of such cases. This makes the careful clinical study all the more important.

This short study has been confined to the cytology. The study of the spinal fluid from a chemical standpoint has not been attempted in this paper, nor has any mention been made of it in the tables. In the tables, however, a few of the more important symptoms and gross findings are tabulated, simply with a view toward showing that the clinical features of these cases also resembled each other very closely.

In conclusion, it is evident, first, that there are many conditions that give the same cytologic findings in the spinal fluid: (a) encephalitis, (b) epidemic myelo-encephalitis, (c) meningismus, (d) tuberculous meningitis, (e) syphilis of the central nervous system; second, that the presence of mononuclear cells or lymphocytes in the spinal fluid cannot be the basis for a diagnosis of tuberculous meningitis; third, that the recovery from animal inoculation, or the finding of the tubercle bacillus microscopically are the only positive means of making the diagnosis of tuberculous meningitis; fourth, that the study of the spinal fluid, although very important, must go hand-in-hand with more careful clinical studies of such border-lying cases as the ones shown in the different tables.

261 Beacon Street.

PROGRESS IN PEDIATRICS

ANATOMY, PHYSIOLOGY AND HYGIENE

Fresh Air Schools

(*J. Perkins. Boston Med. and Surg. Jour., clxiv, 10*)

Fresh air schools are for children physically below par, whether they have latent tuberculosis or not. Due to the active tuberculosis campaign, it has been shown that the majority of these children, and a certain percentage of children who appear in perfect health, have tuberculosis. Children with active tuberculosis should never be permitted in the public schools, but the others, with arrested, apparently cured or latent tuberculosis, can be benefited by the fresh air school. In Providence, R. I., fresh air schools have been conducted for three winters. The school rooms are open to the south. The air in the room is thus as pure as out-of-door air. Foot rugs and chairs with high backs are used to keep the children warm. Caps and mittens are worn. A hot drink is served at 10 o'clock and a lunch at 12. There is a single session, so the children reach home before dark. The homes of the children are visited and instruction in hygiene given. The children almost invariably gain weight, the hemoglobin in the blood rises and the general appearance is markedly improved. RICHARD M. SMITH.

METABOLISM AND NUTRITION

Production of Glycosuria by Epinephrin in Thyroidectomized Dogs

(*F. P. Underhill. Am. Jour. Physiol., 1911, xxvii, 331*)

This work substantiates an earlier one by Underhill and Hilditch, which has been criticized by Falta and Rudinger. They performed another series of experiments on thyroidectomized dogs (the parathyroids were not disturbed) in which they confirmed their earlier findings, that subcutaneous doses of epinephrin (adrenalin chlorid) of 1 mg. per kilo of body weight caused glycosuria.

FRITZ B. TALBOT.

Experimental Contribution to the Study of Tetany in Childhood

(*V. Pexa. Arch. f. Kinderh., liv, Bk. 1-3, p. 1*)

Pexa investigated the cause of tetany and of the "spasmophilic diathesis." Former investigators had attributed the increased irritability of the peripheral nerves present in this disease to a diminution of the calcium present in the body and especially in the brain. Quest had found that an animal on a diet poor in calcium exhibited an increased irritability of the peripheral nerves. The object of Pexa's experiment was to investigate the truth of this finding. He therefore fed a dog for seventy-five days on a diet entirely free from calcium. Another dog of the same age and size was fed on an ordinary diet. From time to time electrical tests were made to determine the irritability of the peripheral nerves in both dogs. At the end of seventy-five days both dogs were killed. The dog on a calcium-free diet did not give any evidence of tetany. The irritability of the peripheral nerves was not increased; the general nervous condition of these dogs was one of marked apathy and stupidity. The brain of the dog which had been fed on a calcium-free diet showed a much smaller amount of calcium than did that of the control animal. Pexa considers that this experiment disproves the two theories proposed before. i. e. (1) that a diet free from calcium will cause an increased irri-

tability of the peripheral nerves and tetany; (2) that a lessened calcium content of the brain will lead to tetany. Pexa thinks that the cause of tetany is to be found elsewhere; that is, in an imperfect action of the parathyroid gland. He examined the parathyroid gland of the dog fed on a calcium-free diet and found no anatomic changes, but found the glycogen content much increased. He comes to the following conclusions: 1. The most striking feature of the clinical picture is a passivity of the animal toward external stimuli. 2. Absolute lack of an increased electrical irritability of the peripheral nervous system. 3. Marked diminution of the calcium content of the central nervous system. 4. Increased glycogen content of the otherwise unchanged parathyroid glands.

G. L. MEIGS.

Malnutrition in Infancy and Its Relation to Gastric Digestion

(*L. J. Tint and L. Breskman. Proc. Path. Soc., Phila., December, 1910, p. 260*)

Malnutrition as a cause of infant mortality occurs commonly in breast-fed as well as in artificially fed infants. Such children, without apparent cause, have green stools, vomiting and loss of weight, which gradually prove fatal. Slight changes in the quality and quantity of the feeding may disturb the delicate balance of the child's digestion and result in an attack of acute indigestion. The quantity of fat in the regular milk-supply may vary from day to day as much as from 4 to 12 per cent., and, in the experience of Tint and Breskman in the children's department of the Philadelphia General Hospital, this variation in the fat resulted in occasional outbreaks of vomiting. Careful preparation of the feedings and regulation of the amount of fat led to a cessation of vomiting. Some children, however, in whom the gastro-intestinal disturbance was well established, continued to vomit and pass green stools, with gradual loss of weight. Gastric lavage relieved the condition in some instances, but in others it failed. In order to ascertain whether free hydrochloric acid was absent in cases of malnutrition the authors analyzed the gastric contents of a number of such cases and compared them with like analyses of the gastric contents of children without gastro-intestinal disturbance. The results were as follows: 1. The examination of the gastric contents of eleven children, mostly under 1 year of age, without vomiting and green stools, showed the constant presence of free hydrochloric acid, rennin and pepsin. 2. Examination of the gastric contents of twenty children under 1 year of age, with green stools, vomiting and gradual loss of weight, showed an absence of free hydrochloric acid, rennin and pepsin. 3. In well-developed cases of malnutrition, such an absence of gastric activity was constant and persisted throughout the course of the affection. They deem the following points worthy of further study: 1. The stomach very early in life plays an important rôle in digestion through its peptic and rennin activities. Free hydrochloric acid is normally present. 2. With the onset of green stools in artificially fed and in breast-fed children, there is an absence of free hydrochloric acid. 3. The absence of gastric activity is relatively constant in children suffering from malnutrition. 4. Milks should be carefully examined for the fat percentage, when that is taken into consideration in making up feedings, particularly in asylums for children.

J. B. C.

The Relation of the Chemical Composition of Human Milk to Chronic Diarrhea and Eczema in Nurslings

(*W. J. Maloney. Practitioner, February, 1911*)

Maloney found that diet and exercise seem to have little or no influence on the sugar and fat content of human milk. Menstruation may coincide with marked impoverishment in fat. The amount of fat in milk varies as the hour and phase of the feed, and also according to individual peculiarities of mothers; a rigorous maternal régime does not appreciably influence the richness of the milk in fat; but an impoverishment may appear simultaneously with the menses.

The lactose of human milk is remarkable for the constancy of its amount, which seems indifferent to feeds, days, régimes and menstrual periods. In sixteen milks examined by Maloney, varying in age from 3 weeks to 7 months, the amount of lactose was only once below 5.28 per cent., and twice above 6.50 per cent. The average age of these milks was 3.12 months, and the average percentage of lactose they contained was 5.82. The percentage of lactose usually attributed to human milk seems, therefore, to be too high. Diarrhea in breast-fed infants whose feeding is carefully directed, may persist in some cases owing to excess of fat in the milk; in others, either owing to the presence of an abnormal laxative principle in milk, or to the undue irritability of an otherwise normal intestinal tract. In none of Maloney's cases could excess of sugar be incriminated. A state of chronic diarrhea prevailed in seven nurslings whose feeding was carefully directed, and whose food was not abnormally rich either in fat or in lactose. Regulation of the mother's régime did not influence this diarrhea. Three to six, usually four, motions occurred daily; they were characteristically of a light yellow color, semi-fluid, inoffensive and without curds. The infants steadily gained in weight, were apparently content, enjoyed an average amount of sleep, and were not unduly querulous. Four of these babies had a history of a persistent tendency to looseness of the bowels from birth. This benign diarrhea resulted, therefore, says Maloney, either from some relatively harmless laxative principle in the mother's milk, or from an excessive irritability peculiar to the infant's intestine. If, on transferring the child for a time to a healthy wet-nurse whose own charge was progressing normally, the diarrhea should cease, the mother's milk would be proved abnormal; if, however, it should continue, the infant's intestine would be proved hypersensitive. The three or four motions each day represented the child's habit. The only treatment required was to discourage weaning and to reassure the mother; for her benefit a little bismuth was usually given to the child. Eczema may arise in nurslings from overfeeding, from richness of the milk in sugar, and from the influence of a faulty maternal hygiene on the chemical composition of the milk. But undoubtedly it may, as in Maloney's six cases, exist in the absence of overfeeding, and when the milk contains only a normal amount of sugar. It may remain unaffected by the sacrifice of all the maternal indiscretions of diet. Probably it may arise independently of its commonly alleged factors; yet the coexistence of diarrhea and eczema in three babies makes Maloney reluctant to exonerate the milk-supply in any case of eczema occurring in a nursling.

F. C. ZAPFFE.

ACUTE INFECTIOUS DISEASES

Treatment of Acute Poliomyelitis

(*W. E. Paul. Boston Med. and Surg. Jour., 1911, clxiv, 46*)

The care of poliomyelitis may be divided into three stages: acute illness, convalescence and the treatment of the permanently damaged structures. In the first stage rest is the one important measure. In the early convalescent period there is a tendency to contracture which must be prevented by splinting, etc. No active measures should be instituted so long as pain continues. The average period of rest is from four to six weeks. In the convalescent stage the chief means of treatment are electricity, active and passive exercises and massage. Electrical treatment must be intelligently given by a physician trained in the use of electrical apparatus. These measures may be kept up with benefit for a year or more.

With the cessation of improvement the condition of permanent crippling is to be considered. Operations and apparatus may do much to improve these deformities.

RICHARD M. SMITH.

Infantile Paralysis

(*R. W. Lovett. Am. Jour. Pub. Hyg., 1910, xx, 875*)

Lovett has studied the epidemics of this disease in this country in relation to means of spreading, etc. It has been stated that the epidemic of 1907 in New York was due to infection brought over from Sweden. It was found on investigation that there was a decided increase in the total immigration just prior to 1907, but a sharp falling off in Scandinavian immigration. It has been repeatedly shown that the disease follows the lines of traffic. The steam and electric railroad travel has greatly increased during the last few years, as shown by statistics of the roads. The increase in automobiles may also be a factor in the situation. The disease occurs in summer, so the question of fruit, dust and insects were investigated. Fruit has not increased it, according to statistics. There has been excessive dryness in the last five years, but not especially in the affected regions. There are no satisfactory data in regard to insects. In general, the epidemic occurs in river valleys and not in coast towns. A small community, affected one year, is likely to be free the next, but this is less applicable to a large area. There is a suggestion of two-year periodicity in the occurrence of the epidemic. It is our duty to advise quarantine and the non-attendance at school of children from affected families.

RICHARD M. SMITH.

Spread of Scarlet Fever and Diphtheria in Schools

(*C. V. Chapin. Amer. Jour. Pub. Hyg., 1910, xx, 813*)

The view is generally held that the intercourse of children in schools is a common cause of the spread of scarlet fever and diphtheria. The author studied the reported cases of these two diseases among school children in Providence for the years 1903-1908. This study showed that scarlet fever exhibited a marked decrease before the summer vacation each year, and that diphtheria decreased in three out of the five years. In half the instances the autumnal increase in the diseases began before the school opened. He concludes that the decrease in these two diseases is associated with temperature changes. A similar study of all cases of scarlet fever and diphtheria for the ten years ending 1903, shows the same lack of connection between the prevalence of the disease and school attendance. Since the incubation period of these diseases is short, if school attendance had any influence on their prevalence, it might be shown even in the short vacations. In Providence there was a decrease of the diseases twenty-one times in the week following the short vacation, an increase twenty-times and the number remained the same eight times. Another reason for doubting that school attendance greatly influences the prevalence of these diseases is that they are more common in children under school age than among those of school age. A tabulation of the cases for twenty years shows an increase for each year of life up to 6, after which there is a yearly decrease. It is quite possible that a certain amount of infection does take place at school, and this should be guarded against by every precaution. Disinfection of the school is useless. The trouble comes from "missed cases" or fever carriers. To prevent harm from them it is necessary to reduce to a minimum the chances of exchange of saliva or other secretions.

RICHARD M. SMITH.

Acute Poliomyelo-encephalitis

(*J. L. Morse. Boston Med. and Surg. Jour., 1911, clxiv, 41*)

Acute poliomyelo-encephalitis is due to an ultra-microscopic organism. The virus is filterable, withstands glycerinization and drying over caustic potash, is not impaired by freezing, but is injured by heating and is destroyed by 1 per cent. H_2O_2 and by menthol. It is doubtful if it has been cultivated outside the body. Inoculation experiments in all warm-blooded animals, except monkeys, have been unsuccessful. Infection has been produced by injections intracerebrally, intraperitoneally, intravenously, into the spinal canal, into large nerves and through

certain mucous membranes, especially of the nasopharynx. The virus escapes through the nasopharyngeal mucous membrane. The disease is contagious, but not highly so. It is probable that the virus gains entrance to the body through the nasopharynx, and it is possible that there may be "carriers" who spread the disease. The period of incubation varies experimentally from three to thirty-three days, the average being eight to nine days. Clinically it may be as short as twenty-four hours. Patients with the disease should be quarantined. Morse has adopted three weeks as the length of time for the quarantine, but it would be of advantage for the State Board of Health to set some arbitrary limit. To prevent the spreading of infection hexamethylenamin should be given to patients during the acute stage of the disease and to persons exposed. The nose of those ill and those exposed should be sprayed with hydrogen peroxid. A second attack is rare, but at present it is not justifiable to attempt to induce active immunity as a protective measure. In general, children should not be taken to places where infantile paralysis exists, or if there, should be kept away from other people. Wherever the virus enters it has a predilection for the nervous system. The vascular lesions constitute the primary cause of the lesions of the nervous tissue. Cellular infiltration changes are set up which are most marked in the perivascular lymph-spaces of the arteries entering the nervous tissue. All parts of the central nervous system may be involved. Our conception of the disease must be enlarged to include acute polio-encephalitis and myelitis. A better term for the disease than poliomyelitis or infantile paralysis would be poliomyelo-encephalitis. Wickman's classification is the best, giving eight forms—the ordinary spinal paralysis; progressive paralysis, usually ascending, including Landry's paralysis; bulbar paralysis; encephalitis, giving spastic, monoplegia or hemiplegia; ataxic form; polyneuritic type; meningitic form and the abortive form. The diagnosis at present is impossible before the appearance of the paralysis. The triad of symptoms—sweating, irritability, and hyperesthesia—are not constant. The leukocyte count is so variable as to be of little value. The diagnosis could be made early by examination of the spinal fluid, but it would be necessary to do lumbar puncture on every sick child in the summer, and this is not a rational procedure. Prognosis as to life and recovery from paralysis cannot be made early in the disease. The treatment during the early stages of the disease consists in giving hexamethylenamin, rest and preventing contractures.

RICHARD M. SMITH.

Observations and Results of Investigation in the Epidemic of Poliomyelitis in Steiermark in 1909

(Karl Potpeschnigg. Arch. f. Kinderh., liv, Bk. 4-6, p. 343)

In August, 1909, the author sent letters to 470 physicians in the province of Steiermark in regard to the epidemic of poliomyelitis which had been raging there during that year. About one-half the physicians answered, reporting about 600 cases; in his own clinic he observed sixty-six cases. He makes them the basis for the following observations:

In regard to contagiousness he observes: 1. In favor of contagiousness are these facts: Very often there are many cases in one family. Neighbors and persons coming in contact with those having the disease are often attacked. Large numbers of cases occur in one neighborhood.

2. Against contagiousness are these facts: There are no cases of epidemics in hospitals. The disease does not develop in many cases in which the contact is very close and long. In many instances there are only isolated cases, although there is no quarantine. He concludes, therefore, that contact infection is very probable, but can only be made certain by the discovery of the cause.

The incubation period he estimates at six to ten days in most cases. The onset and prodromal period were variable in their manifestations. The prodromes were sometimes lacking; the child went to bed well one night and was found paralyzed the next morning. Fever was usually present, ranging sometimes from 102 to 105 F. Sometimes it was normal or low. Tonsillitis in one-

third of his cases was described as occurring before the paralysis. Throat cultures were made in many of the cases; usually a mixed flora was present. In one case a pure culture of the *Staphylococcus albus* was obtained. Gastro-intestinal disturbances were rarer in this epidemic than tonsillitis; the author, however, observed several cases of severe gastro-enteritis. In the cases coming to autopsy Peyer's patches were found swollen. Vomiting was often present.

Leukopenia.—The author saw so few cases in their initial stage that he could not investigate the point of an early leukopenia. In the stage of paralysis the leukocytes were 8,000 to 12,000. The differential blood count showed nothing abnormal.

Initial Nervous Symptoms.—Headache was very often present, localized in the back of the head and very severe. Stiffness of the neck and opisthotonos, with tenderness of the neck muscles were found to be early diagnostic symptoms.

Pain.—Pain was often marked in the peripheral nerves, muscles and joints. Darting pains through the chest and under the shoulder blade were observed several times.

The author concludes that the initial symptoms are so variable as to make an early diagnosis very difficult.

The Stage of Paralysis.—Distinct paralysis was often preceded by a reduction of motor power. Muscular fatigue during this stage seemed to increase the paralysis greatly. Increase and course of the paralysis was often remarkably rapid. He cites a case in which only nine hours elapsed from the beginning of paresis till the death of the patient from paralysis of respiration. These cases early in the epidemic were diagnosed as Landry's paralysis. The spread of the paralysis in other cases was much slower. The paralysis often continued to extend for several days after the temperature had fallen. Paralysis of the bladder often occurred early, but was never permanent. Among his own cases were six cases of vesical paralysis, all connected with paralysis of the lower extremities. Obstipation was noted sixteen times. Pain was marked also during the paralytic stage and led to cramped positions of the limbs and to the development of contractures. Disturbances of sensory, trophic, vasomotor and heat-regulating nerves were often present. There was often increased perspiration, and in several cases desquamation of the skin resembling that after scarlet fever. Facial paralysis was noted six times; most often associated with the cerebral form of the disease, resembling meningitis.

Paralysis of the muscles of deglutition was present only in the rapidly fatal forms. Increase of the deep reflexes was quite often noted. The permanent paralysis affected most often certain groups, as the peronei, deltoid or quadriceps. The lower limbs were much oftener affected than the upper.

Abortive cases were not observed at the clinic, but many were reported from the epidemic. The mortality in this epidemic was 13.1 per cent. For children under school age it was lower—7.5 per cent.; for adults, higher—24.24 per cent. All deaths were from paralysis of respiration. Quite frequently death occurred on the fourth day of the disease.

Lumbar puncture was made forty-eight times on thirty-five children. In all cases a perfectly clear fluid was obtained. On standing, a filmy coagulate, resembling spider's web, was formed. In the majority of cases the protein was increased, the sugar diminished. The pressure of the fluid was often increased and was often so high that the fluid spurted out. The pressure was not measured.

Bacteriologic examinations were made in all cases; in twelve cases Gram-positive diplococci were grown. In two cases the same organism was obtained in smears made from the spinal gray matter. In all other cases the cultures were sterile.

Animal experiments were carried out. Apes, rabbits and guinea-pigs were injected intravenously, intraperitoneally and into the spinal canal with spinal

fluid from cases in the acute and paralytic stages. In no case did paralysis result. Blood cultures were made from several patients. In two cases an organism was obtained similar to that from the spinal puncture. G. L. MEIGS.

GASTRO-INTESTINAL SYSTEM

Proctoscopy and Sigmoidoscopy in Infancy

(*H. L. Bowditch. Arch. Pediat., January, 1911*)

In twenty-four cases of infectious diarrhea, Bowditch examined the rectum and sigmoid by inspection. He found that cases of diarrhea in which there is a history of blood in the stools (especially among infants), show signs of inflammation (red, thickened mucous membrane, prominence of the follicles, ulcers of varying types, but no true membranous condition) throughout the sigmoid and rectum, especially during the acute stage of the disease. These lesions seem to vary, according to the virulence of the infection, as to number and general appearance. They gradually become healed, leaving no signs nor evidence of scar tissue visible to local sigmoidal inspection in life. Bowditch also found that blood and normal intestinal mucous membrane may be present, at least in the sigmoid and rectum, in cases of fermentation diarrhea. Of the severer types of cases all but two patients received one or more irrigations, three had four and two received none. No sign of any healthy appearance was found in these cases, neither did the mucous membrane of those treated, or those untreated, differ in any appreciable way. Of those cases of milder type, all but two patients received silver nitrate irrigations. Three got a single irrigation early in the disease, five had more than two, and at the most, three irrigations. While a gradual improvement was apparent at the end of these repeated irrigations, at no time did the mucous membrane after a single treatment show any distinct betterment.

F. C. ZAPFFE.

RESPIRATORY SYSTEM

The Diagnosis of Pleuritic Effusions in Infancy

(*D. J. M. Miller. Arch. Pediat., January, 1911*)

Miller emphasizes the following points: Pleurisy with effusion is a common affection in infants under 2 years of age. In the vast majority of cases it is purulent. Because of the disastrous, and even fatal, results of delay in or mistakes of diagnosis, it should be recognized early, so that prompt—that is, surgical—treatment may be instituted. The diagnosis is often obscure, demanding, in the highest degree, carefulness, skill and experience. In arriving at a diagnosis, the antecedent affections should be fully appreciated. Of these, pneumonia is by far the most common. The general symptoms, as well as the physical signs, should be carefully weighed and considered. Of these, the latter are the more distinctive. The most reliable signs, in the order of their importance, are (1) exploratory puncture, (2) dulness with a sense of resistance, and (3) displacement of the apex. The other physical signs, so valuable in differentiating effusions in the adult, are uncertain, variable and confusing, and cannot be relied on in infants. The recognition of localized collections of fluid is especially puzzling, and demands great skill and watchfulness and a frequent resort to exploratory puncture or operation. The latter is safe, even when the lung is pierced, and particularly so when fluid is present. Notwithstanding the rare accidents that have followed this procedure, it should be employed to determine the character of the fluid, and, owing to the distressing results of unrecognized empyemas, it is imperatively demanded in all doubtful cases. The variability of the physical signs is a striking feature in infants and should always suggest an effusion.

F. C. ZAPFFE.

BLOOD AND CIRCULATORY SYSTEM

Acute Lymphatic Leukemia in an Infant

(*B. S. Veeder. Arch. Pediat., January, 1911*)

The count in his case, which reached 1,330,000, is the highest leukocyte count which Veeder has been able to find on record in lymphatic leukemia in childhood. E. H., female, aged 17 months, was brought to the hospital for a purpuric eruption, which was said to have appeared five days before admission. Practically no history could be obtained. The child had been breast-fed. A swelling of the neck had appeared "some time" before the eruption. The skin was pale and showed a widespread purpuric eruption, varying in size from small, bright red petechial spots about pinhead in size, to large subcutaneous extravasations, cyanotic in color, and about the size of a 25-cent piece. The large extravasations were present over the forehead, extensor surface of the forearms, the tibiæ, and over the spines of the lumbar vertebræ; the smaller lesions were most marked over the face, right shoulder and legs. Pressure over the bones did not produce pain nor signs of tenderness. The joints were uninvolved. The mucous membranes of the mouth were pale, but showed numerous points of hemorrhage. The saliva was slightly blood-streaked. The tonsils were large, swollen and red, almost shutting off the mouth cavity from the pharynx. The cervical lymph-nodes were enlarged and palpable. They were moderately soft in consistency and about the size of a hickory nut. Pressure over the right side of the neck seemed to cause pain. The axillary and inguinal nodes were both enlarged and distinctly palpable as separate tumors about the size of lima beans. The interesting feature of the case is the blood examination: Hemoglobin, 55 per cent.; erythrocytes, 3,370,000; leukocytes, 1,330,000. The field under the microscope was densely packed with lymphocytes, these being so numerous as to obscure practically everything else. The lymphocytes showed two distinct types, a small and a large cell variety, but between these two extremes there were so many gradations in size that an accurate subdivision of many of the cells into large or small lymphocytes was impossible. The differential count (1,000 cells) was as follows: Lymphocytes, 98.5 per cent.; polymorphonuclears, 1.2 per cent.; myelocytes, .3 per cent. One nucleated red was found during this count.

F. C. ZAPFFE.

NERVOUS SYSTEM

Data and Tests in the Study of the Exceptional Child

(*M. P. E. Groszmann. Brit. Jour. Dis. of Children, vii, 481*)

Apparent disinclination to mind may be due to imperfect hearing; aversion to reading and writing to imperfect vision. Ugliness and irritability may be caused by astigmatism, which, in its turn, produces eye-strain and persistent headaches. Laziness may be a symptom of anemia or neurasthenia, or may be caused by malnutrition or over-exertion at home, lack of sleep or ventilation in the child's sleeping chamber. Fretfulness is often caused by indigestion. Giggling, babbling, whispering, sniffling, restlessness and inattention are often symptoms of some nervous disease. They may be enumerated among the various habit-tics or habit-spasms. Again, momentary inattention and absent-mindedness may be due to a mild form of *petit mal*. Sudden attacks of excitement, outbreaks of temper, destructiveness and hitting of other children, are indications of psychic epilepsy. While true hysteria is not recognized in children, still, emotional temperaments are often seen. Stubbornness and disobedience are danger signs and require further investigation. Realizing that body and mind are two aspects of the same personality, we must first endeavor to establish whether there has been normal growth in either direction. Just as the anatomic structure of a child may be either in advance or behind its years, likewise its mental, moral and volitional development may be accelerated or retarded. Any discrepancy between the stand-

ards of such development for any age is a danger signal. Proper and regularly repeated body measurements are most essential. Recently Professor Rotch has suggested an interesting test by taking *x*-ray pictures of the wrists and hands. The development of the carpal bones and lower epiphysis of radius and ulna are said to be indications of the structural age of a child. Close observations of the various physiologic functions of the body, grip of hand and weakness of any of the special senses, are of great value. Body symptoms will indicate psychic defects; psychic defects will indicate disturbance of physiologic function. The various tests devised by Dr. Sante de Sanctis, Dr. Binet and Groszmann are ingenious methods of measuring motor, sensory and intellectual capacities. The causes of some of the symptoms may be found not so much in the child, but in the home or in the relation of teacher to pupil, or the school curriculum may not be properly graded. The hygiene of the school room, and of the child's life outside of school, require attention. Children who sleep in unhygienic quarters, those who are made slaves outside of the school room and do not get proper rest, cannot possibly have a normal alertness. Children whose progress and conduct is irregular should be transferred to observation groups. Here, under a specially trained nurse and the pediatric expert, the case may be closely watched and inquiry into its family history and surroundings made. The child may be removed to a hospital, sanatorium or special school as the condition requires.

HERBERT J. BALDWIN.

GENITO-URINARY SYSTEM

Albuminuria in Infants

(*Francis Marre. Rev. d'Hyg. et de Méd. Inf., 1910, No. 2, p. 11*)

From a study of the urine of eleven infants less than a month old, Marre concludes that albuminuria in infants, even new-born, indicates a pathologic condition. Children of mothers with eclampsia or albuminuria of pregnancy may show albumin in the urine at birth; or later, secondary to a slight disturbance which would not produce albuminuria in a normal infant. This is believed to be due to a pathologic condition of the kidneys produced by absorption *in utero* of nephrotoxic substances from the mother's blood. With this exception, secondary albuminuria in infants is analogous to the same conditions in adults.

J. HERBERT YOUNG.

OSSEOUS SYSTEM

Enlargement of the Tubercle of the Tibia

(*R. C. Elmshi. Brit. Jour. Child. Dis., viii, No. 85, p. 9*)

Osgood and Schlatter described this condition as due to tearing off of the epiphysis of the tubercle, or a portion of it, by muscular violence. The accounts of the mode of ossification of the tubercle of the tibia vary considerably. Whichever view is correct, it is certain that at the age of 14 the tubercle consists of a tongue-like process extending downward from the anterior part of the upper epiphysis of the tibia and separated from the shaft by a layer of cartilage. This process unites to the shaft from 18 to 24. Complete separation of the tubercle by violence is rare. Enlargement of the tubercle of the tibia in children of 12 to 18 was described by Osgood and Schlatter, as the result of partial separation of the tubercle by muscular violence in jumping and running. It is more common in boys than in girls, and usually comes at 14 to 16. The subjects are often athletes, and the trouble may come on some weeks or months after injury. The complaint is swelling of the tubercle, which is tender on pressure or painful when any exercise is taken in which the quadriceps is exerted powerfully. The pain may even persist at night. The skiagraphic pictures are typical. The pain-

ful condition may last for a few months, or for two years. In many cases the pain recurs at intervals, as a result of exertion of the quadriceps or of slight injury to the tubercle. Eventually the pain subsides, but a permanent enlargement of the tubercle persists. Enlargement of the tubercle may be mistaken for tuberculous disease of the head of the tibia or syphilitic periostitis. Treatment is symptomatic, rest, local anodynes or counterirritants during painful stages. As a rule, the pain subsides in a few months, and the knee may be used as freely as ever, although the swelling persists. HERBERT J. BALDWIN.

THERAPEUTICS

Susceptibility of Animals of Various Ages to Opium Alkaloids

(*E. Döbeli. Monatschr. f. Kinderh., 1910, ix, 397*)

Döbeli used suckling and adult rabbits to determine the relative toxicity of opium in infancy as compared with adults. He concludes from his search through literature and his own experience that opium is not well borne by babies, but that older children probably can take as large doses per kilo of body weight as adults. Suckling rabbits are twice as sensitive to laudanum and morphin as the adult animal. There is no difference in the action of codein on the suckling or the adult. FRITZ B. TALBOT.